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277. *The Orton Rearrangement. Part II.*[1] *The Reactions of Several Substituted* N*-Bromoacylanilides in Various Media causing Rearrangement.*

By M. J. S. Dewar and J. M. W. Scott.

The reactions of a number of *o*-substituted *N*-bromoacetanilides with trichloroacetic acid in chlorobenzene have been studied. Preparations of several new derivatives of *N*-bromoacetanilide are described.

In Part I [1] we described the preparation and rearrangement of *N*-bromo-2 : 6-dimethylacetanilide; this substance showed some unusual properties, owing presumably to the steric influence of the two *o*-methyl groups. We have accordingly examined the rearrangements of a number of *ortho*-substituted derivatives of *N*-bromoacetanilide to obtain further information concerning the steric effects of the substituents and to prepare the way for kinetic studies.

The compounds examined were the *o*-methyl-, *o*-fluoro-, *o*-chloro-, *o*-bromo-, *o*-nitro-, *o*-phenyl, 2 : 4 : 6- and 2 : 4 : 5-trichloro-, and 2 : 6-diethyl derivatives of *N*-bromoacetanilide. Of these the last three compounds and *N*-bromo-*o*-fluoroacetanilide are new; 2-*N*-bromoacetamidodiphenyl had not previously been obtained pure (cf. Scarborough and Waters [2]).

An improved synthesis of *o*-fluoroaniline was devised, namely, oxidation of *o*-fluorotoluene to *o*-fluorobenzoic acid followed by a Schmidt reaction.

All the monosubstituted *N*-bromoacetanilides rearranged smoothly to *p*-bromoacetanilides on treatment with trichloroacetic acid in chlorobenzene, except the nitro-derivative; in this case *o*-nitroacetanilide and *p*-bromochlorobenzene were formed, but normal rearrangement, to 4-bromo-2-nitroacetanilide, took place with trichloroacetic acid in carbon tetrachloride.

The diethyl derivative rearranged normally in boiling water, but gave intractable mixtures with trichloroacetic acid in chlorobenzene. This *N*-bromo-compound was surprisingly unstable, rearranging in the solid state even over phosphoric oxide in a vacuum in the dark.

Both the trichloro-derivatives attacked the solvent, giving free anilide and *p*-bromochlorobenzene.

An attempt to prepare *N*-bromopivalanilide failed; bromination of pivalanilide in acetic acid gave *p*-bromopivalanilide in good yield.

Experimental

2-N-*Bromoacetamidodiphenyl.*—The following modification of Scarborough and Waters's procedure [2] gave a much purer product. 2-Acetamidodiphenyl (10 g.) in warm dioxan (100 ml.) was added slowly with stirring to bromine (10 ml.) and potassium hydrogen carbonate (4 g.) dissolved in 0·25N-sodium hydroxide (2 l.). The yellow precipitate was isolated with chloroform which was then evaporated to a small volume, and hot light petroleum (b. p. 40—60°) was added. 2-*N*-Bromoacetamidodiphenyl separated, on cooling, in yellow prisms (9 g., 68%), m. p. 116—118° (decomp.) (Found : active Br, 27·4, 27·6. Calc. for $C_{14}H_{12}ONBr$: Br, 27·5%).

o-Fluorobenzoic Acid.—*o*-Fluorotoluene (44 g.) and potassium permanganate (75 g.) in water (1·25 l.) were boiled under reflux for 2 hr. Further potassium permanganate (37·5 g.) was then added and heating continued until the permanganate colour had disappeared. After steam-distillation of the excess of fluorotoluene, the solution was filtered and acidified, giving *o*-fluorobenzoic acid (25·6 g., 45%), m. p. 125—126° (lit., 126°).

N-*Bromo-o-fluoroacetanilide.*—*o*-Fluoroacetanilide (5 g.) (from *o*-fluoroaniline [3]) in chloroform (100 ml.) was shaken with an excess of hypobromous acid containing a little mercuric

[1] Part I, Dewar and Scott, *J.*, 1955, 1845.
[2] Scarborough and Waters, *J.*, 1927, 89.
[3] Minor and Van der Werf, *J. Org. Chem.*, 1952, **17**, 1425; Harris, Potter, and Turner, *J.*, 1955, 145.

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oxide. The N-*bromo-amide*, isolated as before, crystallised in needles (3 g., 40%), m. p. 82—84° (Found : active Br, 34·4, 34·3. C_8H_7ONBrF requires Br, 34·4%).

p-*Bromo-o-fluoroacetanilide*.—*o*-Fluoroacetanilide was brominated in acetic acid, and the crude *bromofluoroacetanilide* (1·8 g., 92%) crystallised several times from aqueous alcohol (norite), forming needles, m. p. 158—160° (Found : C, 41·0; H, 3·6; N, 6·0; Br, 34·5. C_8H_7ONBrF requires C, 41·4; H, 3·0; N, 6·0; Br, 34·4%).

N-*Bromo*-2 : 4 : 6-*trichloroacetanilide*.—A solution of 2 : 4 : 6-trichloroacetanilide (15 g.) in chloroform (1·5 l.) was stirred very vigorously with bromine (10 ml.) and potassium hydrogen carbonate (8 g.) dissolved in 0·25N-sodium hydroxide (2 l.). After 1 hr. the N-*bromoanilide* was isolated as before, forming pale yellow prisms (15 g., 60%), m. p. 135—137° (Found : active Br, 25·2. $C_8H_5ONCl_3Br$ requires Br, 25·2%).

N-*Bromo*-2 : 4 : 5-*trichloroacetanilide*, prepared in the same way (50%) yield), crystallised from light petroleum (b. p. 40—60°) in prisms m. p. 96—98° (Found : active Br, 25·0%).

N-*Bromo*-2 : 6-*diethylacetanilide*.—Prepared in the same way as the *o*-phenyl derivative, this N-*bromoanilide* crystallised from light petroleum (b. p. 40—60°) in blades, m. p. 72—75° (Found : active Br, 26·7, 26·2. $C_{12}H_{16}ONBr$ requires Br, 26·6%).

p-*Bromopivalanilide*.—(*a*) *p*-Bromoaniline with pivalyl chloride in pyridine gave crude p-*bromopivalanilide* (2·6 g., 86%) which crystallised from chloroform–light petroleum in needles, m. p. 156—157° (Found : C, 51·8; H, 5·6; Br, 31·2. $C_{11}H_{14}ONBr$ requires C, 51·6; H, 5·5; Br, 31·2%). (*b*) The same compound was obtained in 69% yield by bromination of pivalanilide in acetic acid.

The authors thank Dr. P. M. G. Bavin for a gift of 2 : 6-diethylacetanilide and the corresponding ring-brominated product, Dr. K. N. Ayad for a gift of 2 : 4 : 6-trichloroacetanilide, and Dr. A. Davies for a gift of pivalic acid. One of them (J. M. W. S.) thanks Ipswich Education Committee for a maintenance grant.

QUEEN MARY COLLEGE, MILE END ROAD, LONDON, E.1. [*Received, May 16th,* 1956.]

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278. *The Urea–Formaldehyde Polycondensation. Part I. Kinetics of the Hydrolysis of Methoxymethylurea.*

By A. S. DUNN.

Hydrolysis of methoxymethylurea is catalysed by acids in general and by hydroxyl ions. In alkaline solution the reaction can conveniently be followed by carrying it out in the presence of cyanide, for hydroxymethylurea rapidly decomposes to give formaldehyde which is removed as cyanohydrin, residual cyanide being titrated with mercuric nitrate. In acid solution the decomposition is slower and it is not possible to remove the formaldehyde. There are then consecutive first-order reactions with a second-order reverse reaction : no exact method of treating the results is available for this case but an approximate method is described. The hydrolysis is much retarded by methanol.

EXTENSIVE studies [1] of the reactions between urea, formaldehyde, and their addition compounds, which lead to the formation of aminoplastics, have shown that the addition of formaldehyde to urea is a general acid–base catalysed reaction,[1a] whilst intermolecular condensation of amino- and hydroxyl groups to form methylene-bridged products is catalysed specifically by hydrogen ions.[1b] Rate coefficients of forward and reverse reactions, energies of activation, and equilibrium constants have been evaluated for reactions in aqueous solution. Moreover, it is known that ethers of mono- and di-(hydroxymethyl)-urea with various alcohols can be produced, not only with acid,[2] but also with alkaline catalysts.[3] However, no physicochemical study had been reported of this type of reaction

[1] *E.g.*, de Jong and de Jonge, *Rec. Trav. chim.*, (*a*) 1952, **71**, 643, 661, 890; (*b*) 1953, **72**, 139, 207, 213.

[2] (*a*) Kadowaki, *Bull. Chem. Soc. Japan*, 1936, **11**, 248; B.P. (*b*) 522,643, (*c*) 558,683.

[3] U.S.P. 2,315,745.

until the appearance of a Japanese publication [4] which does not seem very comprehensive. The present paper represents part of a programme undertaken to bring knowledge of the reactions of hydroxymethylureas to parity with that of their self-condensation. Reactions of this type are of technical importance in considering the possibility of cross-linkage of cellulose by urea–formaldehyde resins which are applied to impart crease-resistance to textiles.

Methoxymethylurea is hydrolysed to hydroxymethylurea which decomposes faster to give, ultimately, an equilibrium mixture of urea and formaldehyde.

$$CH_3{\cdot}O{\cdot}CH_2{\cdot}NH{\cdot}CO{\cdot}NH_2 + H_2O \underset{}{\overset{k_1}{\rightleftharpoons}} HO{\cdot}CH_2{\cdot}NH{\cdot}CO{\cdot}NH_2 + CH_3{\cdot}OH \quad . \quad . \quad . \quad (1)$$

$$HO{\cdot}CH_2{\cdot}NH{\cdot}CO{\cdot}NH_2 \underset{}{\overset{k_2}{\rightleftharpoons}} NH_2{\cdot}CO{\cdot}NH_2 + CH_2O \quad . \quad . \quad . \quad . \quad . \quad (2)$$

If cyanide is present, under alkaline conditions it reacts with the formaldehyde and practically prevents the reverse reaction (2) and, at the same time, provides a means of following the reaction :

$$CH_2O + H_2O \underset{}{\overset{k_3}{\rightleftharpoons}} CH_2(OH)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$CH_2(OH)_2 + CN^- \rightleftharpoons HO{\cdot}CH_2{\cdot}CN + OH^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

FIG. 1. *Decrease of rate by addition of sodium nitrate. Initial* $[OH^-] = 0{\cdot}4$. *Initial* $[CN^-] = 0{\cdot}091$; 25°. *I, total ionic strength,* = 1·25 (*A*) *or* 2·0 (*B*).

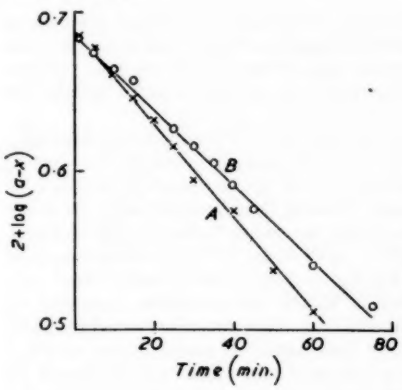
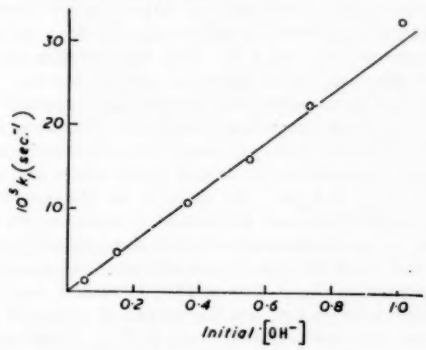


FIG. 2. *Dependence of rate on hydroxyl-ion concentration at* 25°. *Initial ether concn.* = 0·05M. *Initial* $[CN^-] = 0{\cdot}10$N.



RESULTS

Order of Reaction.—The reaction is of the first order. Plots of the logarithm of the ether concentration against time are linear (Fig. 1). First-order rate constants calculated from experiments at different initial ether concentrations are in satisfactory agreement (Table 1).

TABLE 1.

Temp. 25°. Initial $[CN^-] = 0{\cdot}10$M. Initial $[OH^-] = 0{\cdot}55$M.

Initial ether concn. (M)	0·0985	0·0849	0·0479	0·0481	0·0240
$10^5 k_1$ (sec.$^{-1}$)	16·1	16·0	15·5	15·6	15·5

Catalytic Coefficient of Hydroxyl Ions.—The rate increases linearly with hydroxyl-ion concentration (Fig. 2). The rate constant may be written $k_1 = k_0 + k_{OH^-}[OH^-]$. The catalytic coefficient for hydroxyl ions at 25° is $k_{OH^-} = 3{\cdot}00 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$. Hydrolysis of the potassium cyanide does not sensibly increase the hydroxyl concentration even at the lowest hydroxide concentration used.

As will appear below, $k_{CN^-}[CN^-] \sim 10^{-8}$ sec.$^{-1}$, so that the contribution of the cyanide ion to the catalysis is negligible. k_0 is too small to be determined from Fig. 2.

[4] Muraksmi, Sakaguchi, and Akiba, *Bull. Text. Res. Inst.* (*Japan*), 1955, No. 32, 77, 86.

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Energy of Activation.—A plot of log k_1 against $1/T$ is linear. The energy of activation is evaluated as 19·3 kcal./mole. Thus

$$k_{OH^-} = 9{\cdot}46 \times 10^9 \exp(-19{,}300/\boldsymbol{R}T)$$

Effect of Ionic Strength.—Since the rate-determining process in the alkaline hydrolysis of methoxymethylurea is probably a bimolecular reaction between a neutral molecule (the ether)

TABLE 2.

Initial ether concn. 0·05M.	Initial [OH⁻] 0·35N.	Initial [CN⁻] 0·10M.		
Temp.	13°	25°	37°	50°
$10^3/T$	3·50	3·36	3·23	3·10
$10^5 k_1$ (sec.$^{-1}$)	4·00	10·6	41·2	106

TABLE 3.

Temp. 25°. Ionic strength ~1·1. Initial [CN⁻] 0·1M.

x = [HA]/[A]	[HA]	$10k^*$ (sec.$^{-1}$)	pH	10^3[OH]	$10^6(k_{HA} + k_A/x)$
1·0	0	(0·45)	—		
	0·2	1·50	11·19		
	0·5	2·16	11·14	1·5	2·99
	1·0	3·84	11·20		
2·0	0	(0·12)	—		
	0·3	1·12	10·67		
	0·75	2·57	10·61	0·4	2·95
	1·5	5·02	10·60		

and an ion (hydroxyl), no large primary kinetic salt effect is expected. The ionic strength in these experiments is high (often I 0·65) : in the experiments of Fig. 2 the ionic strength varies between 0·15 and 1·10. Fig. 1 shows that the rate of reaction is decreased as the ionic strength is increased by addition of sodium nitrate. In subsequent experiments sodium nitrate was added to maintain the ionic strength constant.

General Acid–Base Catalysis.—Piperidine and piperidinium ion. The catalytic coefficients of the acidic (HA) and basic (A) components of a buffer may be separately evaluated by carrying out experiments at several buffer ratios and concentrations. It can be shown that $k = k_x + \mathrm{HA}(k_{HA} + k_A/x)$. In Table 3, k_x, the rate in absence of buffer, has been obtained from the measured pH and the catalytic coefficient for hydroxyl ions determined above. Then $(k_{HA} + k_A/x)$ has been obtained from a graph of k against [HA]. Solution of simultaneous equations then gives the catalytic coefficient for piperidinium ion $k_{HA} = 2{\cdot}91 \times 10^{-6}$ l. mole^{-1} sec.$^{-1}$, for piperidine $k_A = 0{\cdot}08 \times 10^{-6}$ l. mole^{-1} sec.$^{-1}$. Table 3 clearly demonstrates catalysis by piperidinium ion, but the graphs of k against [HA] at the two buffer ratios are nearly parallel and it is not possible to say that k_A differs significantly from zero. It seems that it may not be possible to detect catalysis by bases weaker than hydroxyl ion. This was confirmed by experiments in which trisodium phosphate was added : no catalytic effect attributable to the phosphate ions could be detected. Thus it is clear that the cyanide ions present in all experiments under alkaline conditions will not exert any catalytic effect.

Hydrolysis in Methanol–Water Mixtures.—The effect of change of solvent on the rate of hydrolysis is illustrated by Fig. 3. There is a marked reduction in the rate of reaction with increasing methanol concentration. The concentration of hydroxyl ions is reduced by addition of methanol because of the equilibrium $OH^- + MeOH \longrightarrow MeO^- + H_2O$. The equilibrium constant for this reaction [5] has a value of about 1. If it is supposed that methoxide ions would not cause hydrolysis, reduction in the hydroxide-ion concentration could account for a reduction in the rate of 13% at most. The major part of the reduction in rate probably arises from change in the polarity of the solvent and, in fact, the results are consistent with a linear relationship between log k_{OH^-} and the reciprocal of the dielectric constant of the solvent, as shown in the inset to Fig. 3.

Hydrolysis in Acid Solution.—Fig. 4 shows catalysis by hydrogen ions. However, neither reaction (4) with cyanide nor any similar reaction by which the formaldehyde formed could be removed occurs in acid solution. Reaction (2) therefore proceeds to equilibrium. Comparison of the rate constants k_1 derived from a first-order plot below 40—50% reaction of the data in

[5] Unmack, *Z. phys. Chem.*, 1928, **133**, 45.

Fig. 4 with those (k_2) calculated from de Jong and de Jonge's values [16] for the decomposition of hydroxymethylurea give ratios of k_2/k_1 of 1·39 in 0·2N- and 1·54 in 1N-nitric acid. This indicates that consecutive-reaction treatment should be applied. Rate constants derived by calculation

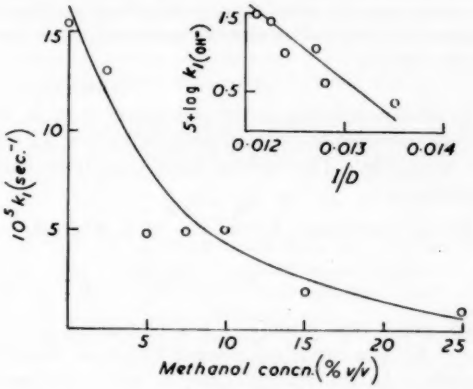

FIG. 3. *Relation between hydrolysis rate constant k_1 and solvent composition at 25°. Initial* [CN^-] = 0·10N. *Initial ether concn.* = 0·05M. [OH^-] + [OMe^-] = 0·50N.

Inset: Linear relation of k_{OH^-} and reciprocal of dielectric constant (D).

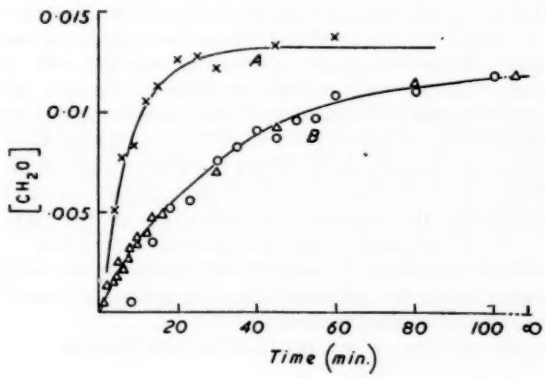

FIG. 4. *Catalysis by hydrogen ions, at 25°. (A)* N-HNO_3; *(B)* 0·2N-HNO_3. ○, △ *Duplicate experiments.*

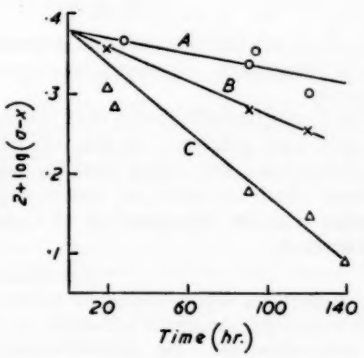

FIG. 5. *Catalysis by acetic acid–acetate buffer, at 25°. Ionic strength* 0·10; pH 4·65. *A, Unbuffered* (pH 4·6); *B,* 0·02N-*acetic acid; C,* 0·06N-*acetic acid.*

allowing for the reverse reaction as above do not differ significantly from those derived by simple first-order treatment of the early part of the curve. The approximate value of k_{H^+} is 1×10^{-3} l. mole^{-1} sec.$^{-1}$.

Catalysis by Acetic Acid.—The results in Fig. 5 show catalysis by acetic acid–sodium acetate buffer solutions. In view of the value derived for the catalytic coefficient for piperidine,

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catalysis by acetate ions which are much more weakly basic may be presumed negligible. An approximate value of $k_1^{HAc} = 2{\cdot}2 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ was derived. From a similar series of experiments on the decomposition of hydroxymethylurea in acetate buffers a value for the catalytic coefficient for acetic acid $k_2^{HAc} = 4{\cdot}3 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ was derived though it is not certain that the effect of the acetate ions is negligible in this case. Thus $k_1^{HAc}/k_2^{HAc} \sim 2$: it appears that consecutive-reaction treatment would be required under all conditions of reaction in acid solution.

Discussion

In alkaline solution, in the presence of cyanide, the reverse reaction (2) can be neglected; the concentration of hydroxymethylurea is at all times small and the reverse reaction (1) is also negligible. The system then comprises only consecutive, irreversible, first-order reactions.

For such a system, $A \xrightarrow{k_1} B \xrightarrow{k_2} C$, where $k_2 = \alpha k_1$, it can be shown that

$$[C]_t = [A]_0\left\{1 + \frac{1}{1-\alpha}\left(\alpha e^{-k_1 t} - e^{-\alpha k_1 t}\right)\right\}$$

It was found that when $\alpha = 3$, a plot of log $(1 - [C]_t)$ against t is concave to the t axis. At $\alpha = 11$, the curvature persists but is so slight that it would be imperceptible experimentally. In the present case, in the conditions in which the overall rate constant is calculated in Table 1 to be $1{\cdot}57 \times 10^{-4}$ sec.$^{-1}$, the rate constant of reaction (2) is calculated from the results of de Jong and de Jonge [1a] to be $1{\cdot}02 \times 10^{-2}$ sec.$^{-1}$: hence $\alpha = 65$. Reactions (3) and (4) are even faster. From the results of Brdička [6] on the rate of dehydration of formaldehyde, together with the value for the equilibrium constant for reaction (3) determined by Biebler and Trümpler,[7] it appears that the catalytic coefficient for the hydration of formaldehyde at 20°, k_{OH^-}, is $5{\cdot}8 \times 10^7$ l. mole^{-1} sec.$^{-1}$: hence $k_3 =$ *ca.* 3×10^7 sec.$^{-1}$. No quantitative information is available about the rate of reaction (4) but it is certainly faster than reaction (2), for it is complete within a minute under analytical conditions whilst 15 min. is necessary for the complete decomposition of hydroxymethylurea under similar conditions. Thus reaction (1) is the rate-determining reaction.

As has been seen above, the rates of reactions (1) and (2) are similar under acid conditions. The case of two consecutive first-order reactions with a second-order reverse reaction does not appear to have been treated in the literature.

The differential equation for the concentration, y, of formaldehyde is of the form

$$dy/dt + f(t)y + ay^2 + g(t) = 0$$

where $f(t)$ and $g(t)$ are functions of t and a is constant. This is a form of Ricatti's equation which can be integrated. However, no rigorous method of evaluating k_1 from the data has been found.

It has been conclusively shown that the hydrolysis of methoxymethylurea is subject to general acid–base catalysis; in this respect the reaction resembles the decomposition of hydroxymethylurea but differs from the condensations between amino- and hydroxymethyl groups which are catalysed specifically by hydrogen ions.[1b] This observation of course implies that the etherification of hydroxymethylurea will be subject to general acid–base catalysis.

Experimental

Hydroxymethylurea was prepared by Walter and Gewing's method [8] except that it was advisable to reduce the amount of potassium hydroxide and to dry the material in a vacuum-desiccator over silica gel. The hydroxymethylurea was recrystallised by dissolution in methanol at $\gtrsim 40°$, followed by cooling in solid carbon dioxide–methanol. The recrystallised material melted sharply at 110° [Found: $CH_2{\cdot}OH$ (hypoiodite method [9]), 35·8; N, 30·2. Calc.

[6] Brdička, *Coll. Czech. Chem. Comm.*, 1955, **20**, 387.
[7] Biebler and Trümpler, *Helv. Chim. Acta*, 1947, **30**, 1860.
[8] Walter and Gewing, *Kolloid-Beih.*, 1931, **34**, 163.
[9] Walker, "Formaldehyde," Reinhold, New York, 2nd. Edn., 1953, p. 385.

for $C_3H_6O_2N_2$: CH_2·OH, 34·4; N, 31·1%]. Fresh preparations dissolved rapidly in methanol and in water, but the solid deteriorated on storage, becoming partially insoluble in methanol and dissolving only slowly in water.

Methoxymethylurea.—Of the suggested methods [2] of preparation that preferred [2b] uses oxalic acid as catalyst which is neutralised by barium hydroxide after dissolution of the hydroxymethylurea. The ether separates on cooling in solid carbon dioxide–methanol and may be recrystallised after dissolution in methanol at room temperature. It then has m. p. 90° (Found: N, 27·25. Calc. for $C_3H_8O_2N_2$: 26·9%). Solid methoxymethylurea was also liable to deteriorate.

Determination of Free Formaldehyde.—The mercuric cyanide method [10] was used to determine free formaldehyde which could usually be equated to hydroxymethylurea under the conditions of the experiments. An indicator consisting of 0·5 g. of diphenylcarbazone per 100 ml., screened with 0·12 g. of Kiton Pure Blue V (C.I. 672) per 100 ml., in 95% ethanol was used.

To 0·1N-potassium cyanide (10 ml.), a sample containing formaldehyde (*ca.* 0·5 mmole) is added, followed by the indicator (8 drops) (brown colour). The solution is acidified to pH about 2 by 2N-nitric acid (apple-green colour: blue-green shade indicates insufficient acid; yellow, excess). The solution is *immediately* titrated with 0·025N-mercuric nitrate. As the end-point is approached the solution is decolorised and, at the end-point, a violet colour is produced which is permanent for at least 3 min. A small blank is required. Mercuric nitrate is standardised against sodium chloride, and potassium cyanide against the mercuric nitrate. Red rubber tubing is not suitable for use with apparatus containing mercuric nitrate solutions but polyvinyl chloride may be used.

Kinetic Experiments.—A solution containing the requisite quantities of methoxymethylurea and potassium cyanide was allowed to attain the working temperature. Experiments were started by running in the requisite amount of sodium hydroxide solution. No free formaldehyde could be titrated in neutral solutions of methoxymethylurea until 2 days after their preparation. Samples were withdrawn at suitable intervals by a pipette fitted with a detachable pipette pump, run into a flask containing the indicator, and acidified immediately.

First-order rate constants were read as the gradients of plots of log $(a - x)$ against t, where a is the initial ether concentration and x the decrease in cyanide concentration.

Mr. K. Anderson assisted with the experimental work.

British Rayon Research Association, Heald Green Laboratories, Wythenshawe, Manchester, 22. [*Received, August 14th*, 1956.]

[10] *Op. cit*, p. 388.

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279. *Steroids. Part XII.* Some Examples of the Favorski Reaction.*

By D. E. Evans, A. C. de Paulet, C. W. Shoppee, and F. Winternitz.

2α-Bromocholestan-3-one undergoes the Favorski reaction to give methyl A-norcholestane-2α-carboxylate accompanied by methyl A-norcholestane-3α-carboxylate, whose structures are proved by Wieland–Barbier degradation respectively to A-norcholestan-2- and -3-one; the latter undergoes inversion to give A-norcoprostan-3-one.

4β-Bromocoprostan-3-one, similarly, by the Favorski reaction yields approximately equal amounts of methyl A-norcoprostane-2β- and -3β-carboxylate, whose structures are proved by Wieland–Barbier degradation to A-norcoprostan-2- and -3-one respectively.

The mechanism of the Favorski reaction is briefly discussed and the configurations of the above four esters are deduced.

One of us and Prins [1] examined the reaction with methoxide ions of the bromo-ketones derived from D-homoandrostan-17*a*-one. Partial separation of the epimeric bromo-ketones was achieved on a small scale, but the work was complicated by the necessity of

* Part XI, *J.*, 1957, 93.

[1] Shoppee and Prins, *J.*, 1946, 494.

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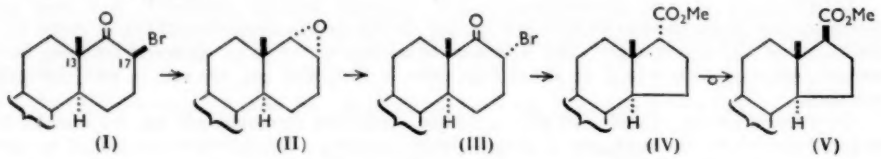
using the mixed epimerides, probably present in approximately equal amounts,[2] for the reaction. The main product isolated was the 17α : 17aα-epoxide (II) derived from the 17β-bromo-ketone [I; Br(axial)], whilst the rearranged ester (V), formed *via* the 17-*iso*-ester (IV) from the 17α-bromo-ketone [III; Br(equatorial)], was produced only in traces.

It appeared that the $C_{(13)}$-angular methyl group might be a factor in the situation, and it was therefore of interest to apply the Favorski reaction to the bromo-ketones derived from cholestan-3-one and coprostan-3-one, which yield respectively only the 2α-epimeride and the 4β-epimeride.[3]



After our work had started we learned from Dr. Winternitz of a parallel investigation at the University of Montpellier; by arrangement we abandoned the application of the Favorski reaction to 2α-bromocholestan-3-one, which had made considerable progress in France,[4] and confined ourselves to the application of the reaction to 4β-bromocoprostan-3-one. The results in both series are now published jointly.

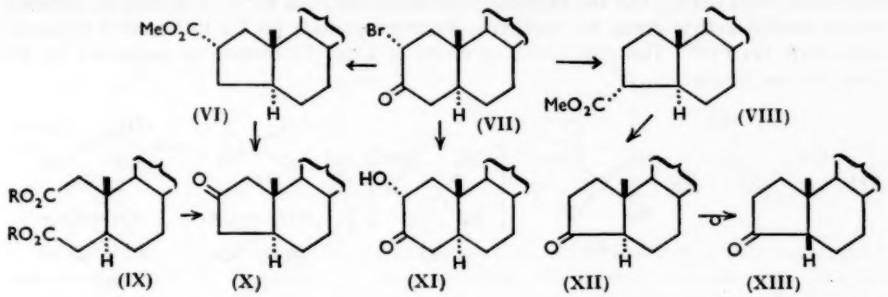
2α-Bromocholestan-3-one (VII) by treatment with sodium methoxide in methanol–ether at 15° affords a mixture of neutral and acidic products. The neutral fraction contains substantial amounts of cholestan-3-one (20—25%), 2α-hydroxycholestan-3-one (XI), and its transformation products (which are being examined by Dr. Winternitz); attention has been directed to the lability of this hydroxy-ketone in alkaline conditions,[5] which was not evident from previous work.[6] The acid fraction, after esterification with diazomethane, affords methyl A-norcholestane-2α-carboxylate (VI) (~25%), accompanied by a relatively small quantity of methyl A-norcholestane-3α-carboxylate (VIII), and dimethyl 2 : 3-*seco*cholestane-2 : 3-dioate (IX; R = Me). When the reaction is carried out in anhydrous ethanol at 15° and the product subjected to alkaline hydrolysis, the acidic fraction is larger, and after re-esterification readily affords the Favorski esters (VI) and (VIII) in approximately equal quantity, together with the dimethyl ester (IX; R = Me).

By a Wieland–Barbier degradation with phenylmagnesium bromide the Favorski ester (VI) gives A-norcholestan-2-one (X), identical with a specimen prepared by pyrolysis of 2 : 3-*seco*cholestane-2 : 3-dioic acid [7] (IX; R = H). The isomeric Favorski ester (VIII), by similar degradation, yields initially the unknown A-norcholestan-3-one (XII), which however undergoes inversion under the experimental conditions to A-norcoprostan-3-one [8] (XIII).

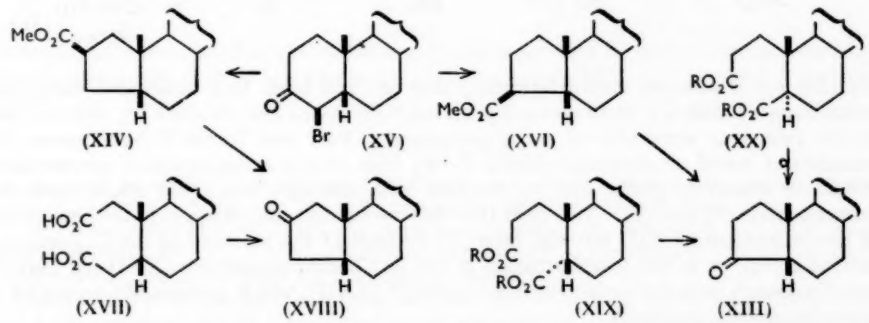
Some of the foregoing results were recorded in a preliminary communication by Winternitz and de Paulet [4] in 1954, which was unfortunately overlooked by Smith and Nace.[9] Smith and Nace obtained the Favorski ester (VI) in a state of purity, but were unable completely to separate the isomeric ester (VIII); they degraded the ester (VI) to A-norcholestan-2-one (X), and from an enriched sample of the ester (VIII) obtained a

[2] Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175.
[3] R. N. Jones, Ramsay, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828; Fieser and Etorre, *ibid.*, 1953, **75**, 1700; Beereboom, Djerassi, Ginsburg, and Fieser, *ibid.*, p. 3500; Corey, *ibid.*, p. 4832; Fieser and Huang, *ibid.*, p. 4837; Cookson, *J.*, 1954, 282; Alt and Barton, *J.*, 1953, 4284.
[4] Winternitz and de Paulet, *Bull. Soc. chim. France*, 1954, 288.
[5] Ruzicka, Plattner, and Furrer, *Helv. Chim. Acta*, 1944, **27**, 727.
[6] Ruzicka, Plattner, and Aeschbacher, *ibid.*, 1938, **21**, 866; Inhoffen and Huang-Minlon, *Ber.*, 1937, **70**, 1695; 1938, **71**, 1720.
[7] Windaus and Dalmer, *Ber.*, 1919, **52**, 162.
[8] Windaus, *ibid.*, p. 170.
[9] Smith and Nace, *J. Amer. Chem. Soc.*, 1954, **76**, 6119.

ketone, m. p. 73—74°, which they described as the unknown A-norcholestan-3-one (XII), but which is clearly A-norcoprostan-3-one (XIII) (our product had m. p. 74°).



4β-Bromocoprostan-3-one (XV) with sodium methoxide in methanol–ether at 15° yielded a neutral fraction containing coprostan-3-one (20%), methyl A-norcoprostane-2β-carboxylate (XIV) (~24%) and methyl A-norcoprostane-3β-carboxylate (XVI) (~24%); the acidic fraction (after esterification) gave a small amount of the Favorski ester (XVI) together with dimethyl 3 : 4-*seco*coprostane-3 : 4-dioate (XIX; R = Me). When the reaction was performed in anhydrous methanol at 15° little or no acidic material was formed,[10] and the yield of Favorski esters (XIV + XVI) increased to 60%; in 98% methanol at 15° it was only 18%.



Wieland–Barbier degradation (phenylmagnesium bromide) of the Favorski ester (XIV) furnished A-norcoprostan-2-one (XVIII), identical with a specimen obtained [11] by pyrolysis of 2 : 3-*seco*coprostane-2 : 3-dioic acid (XVII). Similar degradation of the isomeric ester (XVI) gave A-norcoprostan-3-one (XIII), originally obtained by Windaus [8] by distillation with acetic anhydride of 3 : 4-*seco*coprostane-3 : 4-dioic acid (XIX) or 3 : 4-*seco*cholestane-3 : 4-dioic acid [12] (XX).

The above degradations establish the positions of the methoxycarbonyl groups in the rearranged products (VI), (VIII), (XIV), and (XVI); it seems of interest to examine the mechanism of the Favorski reaction with a view to the elucidation of the configurations of the four esters.

We have previously [1] interpreted the Favorski reaction as a pinacolic change (i) involving the reversible addition (*a*) of an alkoxide ion, with subsequent separation of a halide ion as the rate-determining step and leading to two competing reaction paths, as shown. Path *bc* gives cyclic dimerides of the intermediate (B) and the hydroxy-ketal (D), whilst

[10] Loftfield and Schaad, *J. Amer. Chem. Soc.*, 1954, **76**, 35.
[11] Windaus and Mielke, *Annalen*, 1938, **536**, 116.
[12] Shoppee and Summers, *J.*, 1953, 2528.

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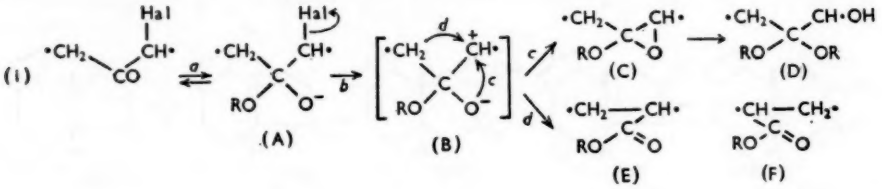
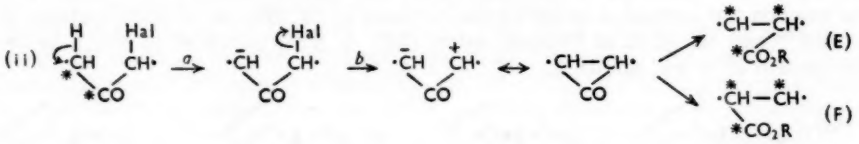
path *bd* affords the rearranged ester (E). The Favorski reaction with ω-chloromethyl *cyclo*hexyl ketone, however, follows path *bc* only in part and also furnishes, not the rearranged ester (as E), but the isomeric rearranged ester (as F); [10,13] similarly, α-chlorobenzyl methyl ketone gives, not methyl α-phenylpropionate (as E), but methyl β-phenylpropionate (as F).[14] The production of esters of type (F) cannot be explained by the pinacolic mechanism.



An alternative mechanism (ii) for the rearrangement was proposed by Loftfield,[15] after his discovery that 2-chloro[1 : 6-^{14}C]*cyclo*hexanone yields a *cyclo*pentanecarboxylic ester (E≡F) in which the isotope has become equally distributed among the positions (*) corresponding to *both* α-carbon atoms of the chloro-ketone. Extraction of a proton by an



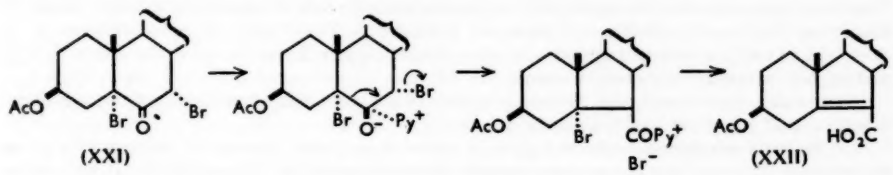
alkoxide ion is now the rate-determining step (*a*), and leads to a mesomeric carbanion which loses a halide ion (*b*) to give a dipolar ion * (cf. Aston and Newkirk [16]), which is one of the resonance structures of a *cyclo*propanone. Burr and Dewar [17] have shown by calculations based on molecular-orbital theory that such a *cyclo*propanone intermediate should be relatively stable and by reaction with alkoxide ions could afford both the isomeric esters (E) and (F). It is clear that this mechanism cannot apply to the conversion of the bromo-ketone (III) into the ester (V) because of the presence of the $C_{(13)}$-angular methyl group, or to the transformation of the 5α : 7α-dibromo-ketone (XXI) (cf. Corey [3] and Cookson [3]) into the unsaturated B-noracid [18] (XXII), which presumably occurs by a pinacolic process, as shown.

Both mechanisms for the Favorski rearrangement lead to the same stereochemical result. In the pinacolic mechanism (i), attack of the electron pair constituting the bond broken, synchronously with the departure of the halogen atom, leads to a linear transition state with *formal* inversion of configuration, but no actual change of orientation

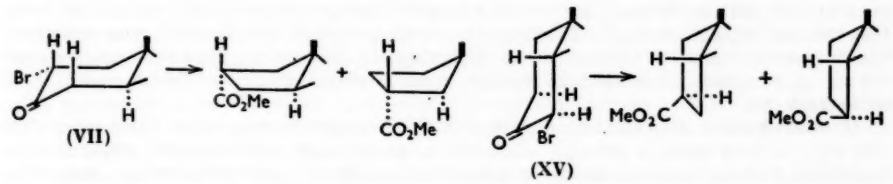
* Professor Dewar (personal communication) has pointed out that in his intermediate [his formula [17] (IV)] all the electrons have their spins paired, and that his formula (IV) must not be taken to represent a diradical with two unpaired electrons with opposed spins. Since this paper was written, another example has been reported by Engel [19]; 3α-acetoxy-17α-bromopregnane-11 : 20-dione affords methyl 3α-acetoxy-17β-methyl-11-oxo-17-*iso*etianate together with the 17α-methyl isomer. The structures of these products have been established by Wendler, Graber, and Hazen,[20] who explain the formation of the second compound by triad cationotropy involving a mobile bromonium ion; it appears however that the Loftfield *cyclo*propanone mechanism (ii) is adequate also for this case.

[13] Mousseron, Jacquier, and Fontaine, *Compt. rend.*, 1951, **232**, 1562.
[14] MacPhee and Klingsby, *J. Amer. Chem. Soc.*, 1944, **66**, 1132.
[15] Loftfield, *J. Amer. Chem. Soc.*, 1950, **72**, 632; 1951, **73**, 4707.
[16] Aston and Newkirk, *ibid.*, *p.* 3900.
[17] Burr and Dewar, *J.*, 1954, 1201.
[18] Woodward and Clifford, *J. Amer. Chem. Soc.*, 1941, **63**, 1123, 2727.
[19] Engel, *ibid.*, 1955, **77**, 1064.
[20] Wendler, Graber, and Hazen, *Chem. and Ind.*, 1956, 847.

if the appropriate hydrogen atom finally remains above the plane of the ring upon which it is situated; the bromo-ketone (III) possessing an equatorial 17-bromine atom with α-configuration furnishes an α-oriented carboxyl group (IV).



In the Loftfield mechanism (ii) the most energetically probable structure for an intermediate *bicyclo*[3 : 1 : 0]hexanone is that in which the bridge involves two distorted " axial " bonds; models suggest that the two " equatorial " C–H bonds at the bridgeheads are approximately collinear. Breakage of either of the bonds adjacent to the carbonyl



group leads in the case of a 3-ketone of the A/B-*trans*-series (VII) to an α-oriented carboxyl group, and in the case of a 3-ketone of the A/B-*cis*-series (XV) to a β-oriented carboxyl group.

Experimental

$[\alpha]_D$ are in $CHCl_3$. Microanalyses marked * were carried out in the microanalytical laboratory of the Université de Montpellier under the direction of Dr. F. Winternitz.

2α-Bromocholestan-3-one (VII) was prepared as described by Butenandt and Wolff,[21] and had m. p. 166—167°, $[\alpha]_D$ +44·5°. Numerous experiments on the reaction with sodium methoxide were carried out, of which the following are typical.

Methyl A-*Norcholestane-2α- and -3α-carboxylate* (VI, VIII).—(*a*) 2α-Bromocholestan-3-one (10 g.), in dry ether (500 c.c.), was added slowly with stirring and cooling to a cold solution of sodium (12·3 g.) in anhydrous methanol (150 c.c.). Precipitation of sodium bromide was immediate, and the mixture was set aside at 15° for 24 hr.; subsequent titration (Charpentier–Volhard) of an aliquot part gave 100% of ionic bromine. The mixture was poured into water, neutralised with 2N-sulphuric (or -acetic) acid, and extracted with ether. One-half of the product (4·3 g.) was esterified with ethereal diazomethane and chromatographed on neutralised aluminium oxide in light petroleum (b. p. 40—60°); elution with light petroleum gave material (1·85 g.) which was submitted to triangular fractional crystallisation from methanol, to yield as the more insoluble product *methyl* A-*norcholestane-2α-carboxylate* (VI), m. p. 94—95°, $[\alpha]_D$ +29° (*c* 3·0) (Found: * C, 80·3; H, 11·5. $C_{29}H_{48}O_2$ requires C, 80·7; H, 11·6%). Fraction B2, m. p. 65—68°, and mother-liquors 1 and 2 were united and rechromatographed, to give by elution with light petroleum (20 c.c. eluates) fractions: C1, oil (20 mg.); C2, crystals (300 mg.); C3, m. p. 44—45° (35 mg.); C4, C5, oils (5 mg., 12 mg.); and use of benzene–light petroleum (1 : 4) gave fractions: C6, m. p. 125—126° (200 mg.); C7, m. p. 125° (90 mg.); C8, C9, crystals (28 mg., 16 mg.). Triangular fractional crystallisation from methanol of C2 yielded finally the ester (VI), m. p. 90—91° (50 mg.), and *methyl* A-*norcholestane-3α-carboxylate*, m. p. 45—46°, $[\alpha]_D$ 0° ± 1° (*c* 1·35) (35 mg.), identical with C3 (Found: * C, 80·3; H, 11·5. $C_{29}H_{48}O_2$ requires C, 80·7; H, 11·6%). Fractions C6—9 consisted of cholestan-3-one (Found: * C, 83·85; H,

[21] Butenandt and Wolff, *Ber.*, 1935, **68**, 2093.

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12·0. Calc. for $C_{27}H_{46}O$: C, 83·9; H, 12·0%) detected by a spot test,† and characterised as the 2 : 4-dinitrophenylhydrazone,[22] m. p. 227—229°, and the semicarbazone,[23] m. p. 236—238°.

The other half (4·3 g.) of the reaction product was hydrolysed with N-methanolic potassium hydroxide on the steam-bath for 2 hr., to yield a neutral (1·87 g.) and an acidic fraction (2·0 g.). The latter was converted by methanolic hydrogen chloride into a crude methyl ester, which by triangular fractional crystallisation furnished the ester (VI) (400 mg.), m. p. 95° (Found : * C, 80·4; H, 11·6%); chromatography of the mother-liquors failed to give the ester (VIII), although a little must have been present.

In another experiment, the 2α-bromo-ketone (6 g.) gave a neutral (3·25 g.) and an acidic fraction (1·57 g.), which yielded similar results.

(*b*) 2α-Bromocholestan-3-one (6·0 g.) was added to a cooled solution of sodium (4·5 g.) in *dry* ethanol (225 c.c.), and the mixture stirred with exclusion of moisture at 15° for 15 hr. After addition of water (30 c.c.), the solution was heated on a steam-bath for 2 hr. to yield, after working up, a neutral (3·8 g.) and an acidic frqction, which by the Fischer–Speier method yielded a crude methyl ester (2 g.). Triangular fractional crystallisation of this from methanol–ether easily afforded the ester (VI), m. p. 94—95° (800 mg.); the last crystalline fraction and the mother-liquor (1·2 g.), by chromatography and elution with light petroleum (20 c.c. eluates), gave fractions : D1, oil (9 mg.); D2, m. p. 59—60° (510 mg.); D3, m. p. 56—60° (140 mg.); D4, D5, m. p. 44—46° (65 mg., 25 mg.), and by use of benzene–light petroleum (1 : 9) D6—9, m. p. 125—126° (20, 135, 80, and 60 mg.). Fractions D2—5, by fractional crystallisation from methanol, readily gave the ester (VIII), m. p. 45° (700 mg.), in a state of considerable purity since the m. p. remained unchanged by further crystallisation. Fractions D6—9 consisted of cholestan-3-one.

Wieland–Barbier Degradation of Methyl A-*Norcholestane-2α-carboxylate.*—The ester (VI) (330 mg.), in pure benzene (30 c.c.), was added to phenylmagnesium bromide, prepared from magnesium (210 mg.) and bromobenzene (2·05 g.) in ether (20 c.c.) at 0° with stirring. After 3 hr. on the steam-bath the complex was decomposed with ice-cold saturated ammonium chloride solution and worked up to yield A-norcholestan-2α-yldiphenylmethanol, m. p. 184—186°. This was dehydrated by refluxing acetic anhydride (5 c.c.) in 2 hr. to 2-diphenylmethylene-A-norcholestane, m. p. 120°, $[\alpha]_D$ −143° (*c* 2·0), after chromatography and crystallisation from acetone–methanol. The olefin (470 mg.) in acetic acid (30 c.c.) was treated with chromium trioxide (300 mg.) in 70% acetic acid (1 c.c.) at 15°. (The olefin was oxidised by chromium trioxide only with difficulty, and in subsequent experiments ozonolysis was found more satisfactory.) The neutral product (300 mg.), isolated in the usual way, was chromatographed on aluminium oxide (3 g.) in light petroleum; elution with light petroleum (2 × 5 c.c.) gave fractions : E1, E2, oils (60, 28 mg.), which crystallised in the cold and consisted of benzophenone, m. p. 48°. Use of benzene–light petroleum (1 : 1) (5 × 5 c.c.) gave fractions E3—7, oils (total 140 mg.), whilst benzene gave fractions E7—10, oils (64 mg.). Fractions E3—7 were reabsorbed on aluminium oxide (6 g.), whereafter elution with light petroleum gave crystals (83 mg.), m. p. 78—95°; two recrystallisations from ether–methanol furnished A-norcholestan-2-one, m. p. and mixed m. p. 95—96°, $[\alpha]_D$ +142° (*c* 1·0), characterised as the semicarbazone, m. p. 230—232°, and 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 166—167°.

Wieland–Barbier Degradation of Methyl A-*Norcholestane-3α-carboxylate.*—The ester was similarly treated with phenylmagnesium bromide to give, successively, *A-norcholestan-3α-yldiphenylmethanol*, m. p. 216—219° after crystallisation from light petroleum (Found : * C, 86·8; H, 10·4. $C_{39}H_{54}O$ requires C, 86·6; H, 10·4%), *3-diphenylmethylene-A-norcholestane*, m. p. 143—144° after crystallisation from ethanol–ether–light petroleum (Found : * C, 89·7; H, 9·95. $C_{39}H_{54}$ requires C, 89·6; H, 10·4%), and by ozonolysis and reduction of the ozonide with zinc–acetic acid A-norcoprostan-3-one, m. p. and mixed m. p. 73°, $[\alpha]_D$ +104° (*c* 2·0), characterised as the semicarbazone, m. p. 268—270°, and 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 159—160° (Found : * C, 69·4; H, 8·7. Calc. for $C_{32}H_{48}O_4N_4$: C, 69·5; H, 8·75%).

4β-Bromocoprostan-3-one (XVII).—Coprostan-3-one, prepared as described by Butenandt

† The product (several μg.) is dissolved in chloroform, and a drop deposited on Whatman chromatographic paper; the strip, after drying in a current of air, is sprayed with a freshly prepared methanolic-hydrochloric acid solution of 2 : 4-dinitrophenylhydrazine. A yellow spot, not removed by a dilute acidic solution of sodium nitrite, indicates a ketone.

[22] Djerassi, *J. Amer. Chem. Soc.*, 1949, **71**, 1007.
[23] Dorée and Petrow, *J.*, 1935, 1391.

and Wolff,[21] failed to crystallise from the reaction mixture which was therefore poured into saturated sodium hydrogen carbonate solution. The precipitated solid was filtered off and dried in the absence of light to furnish 4β-bromocoprostan-3-one, m. p. 106—108°, $[\alpha]_D$ +53° (*c* 0·6) (cf. lit.,[21] m. p. 111°).

Methyl A-*Norcoprostane-2β- and -3β-carboxylate* (XIV, XVI).—(*a*) 4β-Bromocoprostan-3-one (5 g.) in anhydrous ether (200 c.c.) was added dropwise to sodium methoxide in methanol [prepared from anhydrous methanol (300 c.c.) and sodium (6·2 g.)] at 15°; precipitation of sodium bromide occurred immediately and the solution was kept overnight at 15°. After acidification of the reaction mixture with 2N-sulphuric acid, extraction with ether gave an ethereal solution from which no acid was extracted by 2N-sodium hydroxide. Evaporation of the dry ethereal solution gave an opaque solid, which afforded a precipitate when triturated with ether. Collection of the sodium salt, acidification of its aqueous suspension, and extraction with ether in the usual manner furnished a yellow viscous oil which was esterified with ethereal diazomethane. Isolation of the methyl esters in the usual manner yielded an oil (1·39 g.). The ethereal mother-liquors from the filtration of the sodium salt were washed with water, dried, and evaporated, to afford an oil (2·87 g.).

The methyl esters (1·39 g.) obtained from the acidic fraction were chromatographed on neutral aluminium oxide (40 g.; reactivated at 180°/10 mm. for 2 hr.). Elution with pentane (3 × 130 c.c.) gave fractions A1—3, oils (559 mg.). Further elution with pentane (4 × 130 c.c.) yielded fractions A4—7, oils (409 mg.), which by crystallisation from methanol–ether gave needles of *methyl* A-*norcoprostane-3β-carboxylate* (XVI), m. p. 66—67° [Found (after drying at 40°/0·03 mm. for 10 hr.): C, 80·45; H, 11·2. $C_{28}H_{48}O_2$ requires C, 80·75; H, 11·5%]. Elution with benzene–pentane (1 : 9 and 1 : 4) gave fractions A8 and A9 as oils (294 mg.) which slowly crystallised and by recrystallisation from methanol–ether furnished dimethyl 3 : 4-*seco*coprostane-3 : 4-dioate (XIX; R = Me), m. p. 60—61°.

Fractions A1—3 (559 mg.) were rechromatographed on neutral aluminium oxide (20 g.). Elution with pentane (10 × 20 c.c.) furnished oily fractions B1—10 (550 mg.), each fraction having $[\alpha]_D$ +46° ± 2°.

The neutral fraction (2·87 g.) was chromatographed on neutral aluminium oxide (81 g.). Elution with pentane (6 × 250 c.c.) furnished fractions C1—6 as oils (984 mg.). Elution with benzene–pentane (1 : 9; 3 × 250 c.c. and 1 : 1; 6 × 250 c.c.) afforded oily fractions C7—15 which by crystallisation from methanol–acetone gave coprostan-3-one, m. p. and mixed m. p. 61—62°. Elution with benzene, ether, and chloroform gave a yellow oil (480 mg.), which was not further examined.

Fractions C1—6 were rechromatographed on neutral aluminium oxide (60 g.). Elution with pentane (10 × 100 c.c.) gave D1—10 as mobile oils, which did not crystallise or solidify at −80°. Distillation of the oil at 170°/0·03 mm. afforded a mixture of methyl A-norcoprostane-2β- (XIV) and -3β-carboxylate (XVI), $[\alpha]_D$ +44° (*c* 1·1) (Found: C, 80·8; H, 11·5. Calc. for $C_{28}H_{48}O_2$: C, 80·75; H, 11·5%).

The yields were thus: Favorski esters 48%, dimethyl 3 : 4-*seco*coprostane-3 : 4-dioate 3%, and coprostan-3-one 20%.

(*b*) 4β-Bromocoprostan-3-one (5 g.) in ether (200 c.c.) was added dropwise to a solution of sodium methoxide in methanol [prepared from anhydrous methanol (292 c.c.), water (8 c.c.), and sodium (6·2 g.)] at 15°; precipitation of sodium bromide occurred immediately and the solution was kept overnight at 15°, then worked up as in the previous experiment, to furnish the mixed Favorski esters (XIV, XVI) (833 mg., 17·5%), coprostan-3-one (897 mg., 18·7%), and dimethyl 3 : 4-*seco*coprostane-3 : 4-dioate (134 mg., 2·8%).

(*c*) 4β-Bromocoprostan-3-one (4·2 g.) in anhydrous ether (120 c.c.) was added dropwise to a solution of sodium methoxide in methanol [prepared from methanol (150 c.c.) and sodium (5 g.)] at 15°; precipitation of sodium bromide occurred immediately and the solution was kept for 30 hr. at 15°. The ether was removed and after the addition of water (20 c.c.) the mixture was refluxed for 1 hr. Acidification with 2N-sulphuric acid and extraction with ether gave an ethereal solution which was washed with water, dried, and evaporated to a yellow oil (3·94 g.). The oil was esterified with ethereal diazomethane, and the product, isolated in the usual manner, treated with Girard's reagent T (200 mg.) in refluxing ethanol (90 c.c.) and acetic acid (10 c.c.) for 1 hr. The solution was diluted and extracted with ether, to give an ethereal solution which was washed with sodium hydrogen carbonate solution and water. Regeneration of the ketonic material from the aqueous layer by acid hydrolysis afforded coprostan-3-one, m. p. 61—62°

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(700 mg.). Evaporation of the dry ethereal extracts furnished a yellow oil (3·22 g.) which was chromatographed on neutral aluminium oxide (90 g.). Elution with pentane gave as a colourless oil (1·1 g.), $[\alpha]_D$ +47° (*c* 0·86), a mixture of methyl A-norcoprostane-2β- and -3β-carboxylate. Elution with benzene–pentane (1 : 4) gave an oil (200 mg.), which by crystallisation from methanol–ether furnished dimethyl 3 : 4-*seco*coprostane-3 : 4-dioate (XIX; R = Me), m. p. 60—61°. Elution with ether, chloroform, and methylene dichloride furnished a yellow oil (1 g.). The yields of product were thus: Favorski esters 28%, dimethyl-3 : 4-*seco*coprostane-3 : 4-dioate 5·2%, and coprostan-3-one 18·5%.

(*d*) 4β-Bromocoprostan-3-one (4·5 g.) was added to a vigorously stirred solution of sodium methoxide in methanol [prepared from anhydrous methanol (150 c.c.) and sodium (5 g.)] at 15°. Stirring was continued for 30 hr., and after the addition of water (20 c.c.) the solution was refluxed for 1 hr. The product (4·2 g.) isolated as in the previous experiment was esterified with ethereal diazomethane and the ketonic material was removed with Girard's reagent T. Regeneration of the ketone from the aqueous layer afforded an oil (480 mg.), which by crystallisation from methanol–acetone furnished coprostan-3-one, m. p. 60—61°.

The non-ketonic material (3·7 g.) was chromatographed on neutral aluminium oxide (120 g.). Elution with pentane gave, as a colourless oil E (2·57 g.), $[\alpha]_D$ +45° (*c*, 1·0), a mixture of methyl A-norcoprostan-2β- and 3β-carboxylate [Found (after drying at 100°/0·03 mm. for 3 hr.): C, 80·6; H, 11·5. Calc. for $C_{28}H_{48}O_2$: C, 80·75; H, 11·5%]. Elution with benzene–pentane (1 : 4) furnished an oil (210 mg.), which by crystallisation from methanol–ether gave dimethyl 3 : 4-*seco*coprostane-3 : 4-dioate (XIX; R = Me), m. p. 60—61°. Elution with ether and chloroform gave an unidentified oil (1·0 g.). The oil E (2·57 g.) was rechromatographed on neutral aluminium oxide (90 g.). Elution with pentane (10 × 100 c.c.) furnished a series of oily fractions, all having $[\alpha]_D$ +45° ± 2°. The yields of products were thus: Favorski esters 61%, dimethyl 3 : 4-*seco*coprostane-3 : 4-dioate 11%, and coprostan-3-one 5%.

2- *and* 3-*Diphenylmethylene-*A*-norcoprostane.*—The mixed esters (XIV, XVI) (1·8 g.) in anhydrous benzene (120 c.c.) were added to phenylmagnesium bromide in ether [prepared from bromobenzene (8·4 c.c.), magnesium (1·62 g.), and ether (120 c.c.)]. The solution was refluxed for 5 hr., cooled, poured into ice-cold saturated ammonium chloride solution, and extracted with ether. Steam-distillation of the benzene–ether layer removed diphenyl, and the residual oil, obtained in the usual manner, was refluxed with acetic acid (120 c.c.) and acetic anhydride (60 c.c.) for 3 hr. Removal of the solvent under reduced pressure afforded a yellow oil (1·7 g.) which was chromatographed on aluminium oxide (50 g.). Elution with pentane (3 × 150 c.c.) furnished a colourless oil (1·7 g.), $\lambda_{max.}$ 252 mμ (log ε 4·1 in EtOH).

A-*Norcoprostan-3- and -2-one.*—The above oil (1·0 g.) in ethyl acetate was treated with a stream of ozonised oxygen at −70° for 30 min. The solution was set aside at room temperature for 1 hr., and the solvent removed under reduced pressure. The residual oil was treated with zinc dust (10 g.) in refluxing acetic acid (200 c.c.) for 2 hr., and after removal of solvent at 10 mm. and then at 0·03 mm. the residue (820 mg.) was chromatographed on aluminium oxide (30 g.). Elution with benzene–pentane (1 : 9; 3 × 100 c.c.) furnished oily fractions F1—3 (220 mg.), and benzene–pentane (1 : 4) afforded an oily fraction F4 (250 mg.). Elution with benzene–pentane (1 : 1) gave an unidentified fraction F5, m. p. 182° (305 mg.). Fractions F1—3 were rechromatographed on aluminium oxide (8 g.); elution with benzene–pentane (1 : 9; 5 × 30 c.c.) furnished an oil (210 mg.), which by crystallisation from methanol gave A-norcoprostan-3-one (XIII), m. p. and mixed m. p. 73—74°, $[\alpha]_D$ +102° (*c* 1·2). Further elution with benzene–pentane (1 : 4) gave an oil (5 mg.). Fraction F4 was rechromatographed on aluminium oxide (8 g.); elution with benzene–pentane (1 : 9 and 1 : 4) gave a solid (215 mg.) which by recrystallisation from methanol–ether afforded A-norcoprostan-2-one (XVIII), m. p. 101—103°, $[\alpha]_D$ +46° (*c* 2·0).

Methyl A-norcoprostane-3β-carboxylate [from (*a*), p. 1457] was degraded as in the previous experiment, to furnish only A-norcoprostan-3-one (XIII), m. p. 73—74°.

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UNIVERSITÉ DE MONTPELLIER, INSTITUT DE CHIMIE.
UNIVERSITY OF WALES, UNIVERSITY COLLEGE, SWANSEA. [*Received, September 24th*, 1956.]

280. *Detection of the Epoxide Group by Infrared Spectroscopy.*

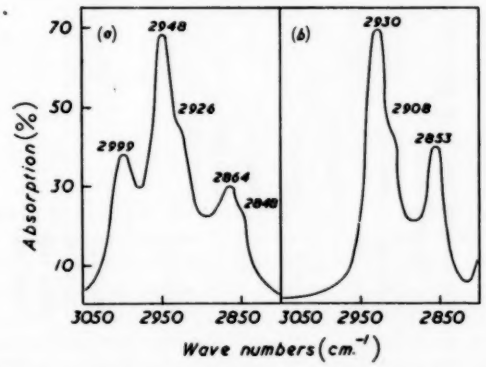
By H. B. Henbest, G. D. Meakins, B. Nicholls, and K. J. Taylor.

For partially alkylated ethylene oxides of moderate molecular weight a characteristic C–H stretching band can be detected in the 3050—2990 cm.$^{-1}$ region of the infrared spectrum. Correlations between band position and epoxide structure are discussed.

The need for reliable methods of diagnosing the presence of epoxide groups in organic molecules has prompted many efforts to utilise infrared measurements for this purpose.[1] Various regions of the spectrum between 1300 and 650 cm.$^{-1}$ have been studied but, although some success has been achieved in relating certain bands to various types of epoxide structures, no general correlations have emerged. The reasons for this failure have been discussed.[1c]

Recent work on a related problem, detection of the *cyclo*propane group,[2] has shown that more reliable information can be obtained from the 3000 cm.$^{-1}$ region. It is known that decreasing the ring size of alicyclic systems increases the C–H stretching frequencies of the constituent methylene groups, and in derivatives of *cyclo*propane this leads to stretching bands sufficiently well separated from the main C–H absorption to appear as distinct peaks at about 3045 cm.$^{-1}$. With this in mind we examined the spectra of epoxides shown in the Table over the 3200—2800 cm.$^{-1}$ region.

Table.—Most of the compounds were examined in CCl_4 solution on a Perkin-Elmer model 21 double-beam spectrometer fitted with a calcium fluoride prism : those marked * refer to CS_2 solutions and a sodium chloride prism. (The close correspondence between the results for a few cases studied under both conditions shows that the higher resolution of a calcium fluoride prism is not necessary for the correlations discussed below.) The figures in parentheses are molecular extinction coefficients (mole^{-1} l. cm.$^{-1}$). No intensity values are given for shoulders (sh) on the sides of main bands.



a, 1 : 2-*Epoxy*cyclo*hexane*.
b, cyclo*Hexane*.

Compounds 1—7 have a 1 : 2-disubstituted epoxide group attached to an acyclic nucleus (Ia) or to a *cyclo*hexane ring (Ib), and in each case there is a separate peak (~3000 cm.$^{-1}$) on the high-frequency side of the main group of C–H stretching bands (2985—2850 cm.$^{-1}$). This peak is absent in corresponding substances lacking the epoxide function, as is made clear (see Figure) by comparing *cyclo*hexene oxide (no. 4) with *cyclo*hexane. When the

[1] See, *inter al.*, (*a*) Field, Cole, and Woodford, *J. Chem. Phys.*, 1950, **18**, 1298; (*b*) Shreve, Heether, Knight, and Swern, *Analyt. Chem.*, 1951, **23**, 277; (*c*) Günthard, Heusser, and Fürst, *Helv. Chim. Acta*, 1953, **36**, 1900; (*d*) Patterson, *Analyt. Chem.*, 1954, **26**, 823.

[2] For leading references see (*a*) Wiberley and Bunce, *ibid.*, 1952, **24**, 623; (*b*) Slabey, *J. Amer. Chem. Soc.*, 1954, **76**, 3604; Cole, *J.*, 1954, 3807, 3810.

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Infrared frequencies (cm.$^{-1}$) of epoxides (intensities in parentheses).

No.	Compound	Epoxide bands		Other CH stretching bands					
1	1 : 2-Epoxypropane (III; R = H)	3050 (30)	3000 (60)	2975 sh		2931 (30)			
2	1 : 2-Epoxy-2-methylpropane (III; R = Me)	3045 (30)		2981 (70)	2972 (75)	2935 (40)	2922 (40)		
3	*trans*-3 : 4-Epoxyhexan-1-ol *		2990 (110)		2955 (80)		2905 (40)		
4	1 : 2-Epoxy*cyclo*hexane		2999 (80)			2948 (190) 2926 sh		2864 (60) 2848 sh	
5	*cis*-2 : 3-Epoxy*cyclo*hexanol		3004 (45)			2949 (105)		2866 (35) 2850 sh	
6	3 : 4-Epoxy*cyclo*hexanol * †.....		3002 (60)			2942 (95)			2858 (20)
7	3 : 4-Epoxy*cyclo*hexyl acetate * †		2995 (55)		2955 (55)				
8	1 : 2-Epoxy*cyclo*pentane	3037 (45)		2980 sh	2963 (80)	2927 (55)			2856 (25)
	bicyclo[2 : 2 : 1]*Heptane derivatives* (IV).								
9	R = OH *	3033 (35)		2975 (125)			2910 (50)		
10	R = OAc *	3031 (35)		2977 (115)				2880 (15)	
11	R = CO_2Me *	3029 (40)			2955 (205)	2940 sh			2871 (25)
12	R = CH_2·OAc *	3031 (45)			2970 (140)			2880 (40)	
	Steroids.								
13	2α : 3α-Epoxycholestane	Not detectable			2955 sh	2939 (635)			2874 (250) 2856 sh
14	5α : 6α-Epoxycholestane	,,	,,			2940 (670)	2910 sh		2868 (320)
15	5β : 6β-Epoxycholestane	,,	,,			2945 (645)	2915 sh		2870 (320)

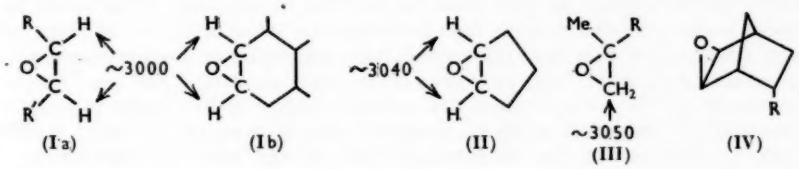
* NaCl prism, CS_2 solution. † Mixture of *cis* and *trans* isomers.

Materials: Nos. 3, 6, 7 and 9—12, Henbest and Nicholls, unpublished work; 5, Henbest and Wilson, *Chem. and Ind.*, 1956, 659; the remainder were prepared by published methods.

oxide group is fused to a five-membered ring (II) (nos. 8—12) a similar characteristic band appears, but at higher frequency (~3035 cm.$^{-1}$). [Formulæ (Ia), (Ib), and (II) are used to represent compounds 1—12, the *bicyclo*heptane group being considered for the present purpose as more closely related to *cyclo*pentane than to *cyclo*hexane.]

From the Figure it can be seen that the epoxide band is superimposed on a rising background which develops into the main C–H stretching bands. It is to be expected therefore that as the relative intensity of the main group increases, it will be more difficult to pick out the epoxide band. An example of this increase occurs when the epoxide ring is included in polycyclic systems such as steroids (compounds 13—15). Here there are more methyl and methylene groups for each epoxide unit and at comparable concentrations the epoxide peak is " swamped " by the main (broad) C–H bands which, although reaching their maxima below 2950 cm.$^{-1}$, have strong and rapidly rising absorptions at 3000 cm.$^{-1}$. Thus the failure to detect an epoxide band in 2α : 3α-epoxycholestane (Ib; no. 13) is not surprising : it does, of course, limit the applicability of the correlation to compounds with a reasonable (at present, unspecified) epoxide : methyl–methylene ratio.

Although the vibrations responsible for the epoxide bands listed in the Table cannot be identified with certainty the results show that systematic correlations between band position and epoxide environment are to be expected. Probable assignments (see formulæ) can be developed as follows. The epoxide bands almost certainly arise from the C–H stretching vibrations of methylene and methine groups contained in epoxide rings (*i. e.*, $-CH_2 \cdot O-$ and $>CH \cdot O-$). In compounds 3—7 the epoxide rings are connected to unstrained systems and contain only the latter (methine) type of group. The band occurring at about 3000 cm.$^{-1}$ in each case may then be ascribed to epoxy-methine C–H stretching. When the methine groups are linked to the more strained *cyclo*pentane and



*bicyclo*heptane nuclei (compounds 8—12) the frequency is raised to 3040—3030 cm.$^{-1}$. This increase is paralleled by a similar situation found in the olefinic C–H stretching frequencies of different types of 1 : 2-disubstituted *cis*-ethylenic centres : thus acyclic *cis*-olefins and *cyclo*hexene derivatives give bands near 3020 cm.$^{-1}$, whereas *cyclo*pentene and *bicyclo*heptene compounds absorb at higher frequencies (3075—3045 cm.$^{-1}$).[3]

The frequencies of these epoxy-methine bands are higher than those of normal methine groups which have weak stretching bands around 2900 cm.$^{-1}$. Two separate factors may contribute to this effect, *viz.*, inclusion of the methine group in a three-membered ring, and direct attachment to oxygen. [That an increase should be caused by placing the methine group in a small ring is reasonable by analogy with the corresponding shifts in the bands of cyclic methylene groups.[4] Support for the oxygen's effect is found in the higher frequencies of methine groups in acyclic ethers ($>CH \cdot O-$) than for hydrocarbons.[5]]

Propylene oxide (no. 1) containing a methine and a methylene group in an epoxide ring gives two peaks. From the results with compounds 1—5 it seems reasonable to associate the 3000 cm.$^{-1}$ band again with the methine group : the intensity of the band is approximately half that shown by the other open-chain epoxide (no. 3) containing *two* methine groups. The second band (3050 cm.$^{-1}$) of propylene oxide corresponds closely with the single peak (3045 cm.$^{-1}$) of *iso*butylene oxide (no. 2), and the bands are therefore attributed

[3] Henbest, Meakins, Nicholls, and Wilson, *J.*, 1957, 997.
[4] Roberts and Chambers, *J. Amer. Chem. Soc.*, 1951, **73**, 5030.
[5] Pinchas, *Analyt. Chem.*, 1955, **27**, 2.

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to the epoxy-methylene group present in both compounds. It is to be noted that such a simple analysis cannot be applied to a highly symmetrical molecule such as ethylene oxide where the C–H vibrations are strongly coupled. Thus ethylene oxide, previously studied in the vapour state,[6] gives a complex spectrum in CCl_4 solution with bands at 3018 (35), 3002 (35), 2959 (10), and 2922 (20) cm.$^{-1}$.

We are grateful to the Department of Scientific and Industrial Research for a grant to one of us (B. N.) and to Miss W. Peadon for technical assistance.

THE UNIVERSITY, MANCHESTER, 13. [*Received, October 10th*, 1956.]

[6] Thompson and Cave, *Trans. Faraday Soc.*, 1951, **47**, 946.

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281. *The* C–H *Stretching Bands of Methoxyl Groups.*

By H. B. HENBEST, G. D. MEAKINS, B. NICHOLLS, and A. A. WAGLAND.

Methoxyl groups in organic compounds can be detected by a characteristic band in the 2832—2815 cm.$^{-1}$ region of the infrared spectrum.

THE pioneering work of Fox and Martin [1] on the CH stretching frequencies of methyl, methylene, and methine groups has been extended in recent years by some careful studies of the 3000 cm.$^{-1}$ region of hydrocarbons.[2] Within a restricted field—for example, saturated aliphatic hydrocarbons [2b]—spectra can be analysed fairly exactly in terms of the CH stretching vibrations of non-interacting $-CH_3$, $>CH_2$, and $\gtrless CH$ units. But with most organic compounds this simple idea cannot be applied: [3] the complex spectra are difficult to interpret and so far their main use has been in detecting olefinic bonds by the presence of peaks or shoulders on the high-frequency side of the main CH stretching bands.

In an attempt to obtain more information from this region of the spectrum a series of methyl ethers shown in the Table have been studied over the 3100—2800 cm.$^{-1}$ range.

Comparison of the methyl ethers and reference compounds (Table) provides clear evidence that the methoxyl group is associated with a characteristic band G (2832—2819 cm.$^{-1}$) appearing on the low-frequency side of the main CH absorption. The appearance of the spectra of three compounds containing no methyl, a *C*-methyl, and an *O*-methyl group respectively, is illustrated in the Figure. It is important that band G is not given by *C*-methyl groups (cf. nos. 1 and 2, 4 and 5) or by ethoxyl groups (cf. nos. 12 and 13, 14 and 15, 21 and 22). For compounds nos. 2, 3, 6—9, 13, 15, and 16, which are of roughly comparable molecular weight and have each one methoxyl group, the intensity of band G is between 35 and 75 units; with two methoxyl groups (nos. 10 and 11) the intensity is about 120 units. It is noteworthy that the band still appears in methoxy-steroids (nos. 18—20) where the ratio of OMe to CH_2 and *C*-Me groups is much lower than in the acyclic and monocyclic examples. (Compare the behaviour of steroid *vic.*-epoxides [4] where the characteristic epoxide band is swamped by the main CH absorptions.) The correlation should be useful in supplementing the detection of methoxyl groups by a band near 1100 cm.$^{-1}$ recently studied in methoxy-steroids by Page.[5]

The simplest analysis of paraffinic CH stretching bands involves consideration of four main vibrations, *viz.*, antisymmetric and symmetric CH stretching of methyl and methylene groups. (The CH band of the methine group at about 2890 cm.$^{-1}$ is variable in frequency and weaker than the others.) In aliphatic systems the bands are near 2960, 2870 cm.$^{-1}$ (CH_3) and 2925, 2850 cm.$^{-1}$ (CH_2).[2b] While four (and only four) peaks are

[1] Fox and Martin, *Proc. Roy. Soc.*, 1938, *A*, **167**, 257; 1940, *A*, **175**, 208.
[2] (*a*) Plyler and Acquista, *J. Res. Nat. Bur. Stand.*, 1949, **43**, 37; Francis, (*b*) *J. Chem. Phys.*, 1950, **18**, 861; (*c*) *Analyt. Chem.*, 1952, **24**, 604; 1953, **25**, 1466.
[3] Pozefsky and Coggeshall, *ibid.*, 1951, **23**, 1611.
[4] Henbest, Meakins, Nicholls, and Taylor, preceding paper.
[5] Page, *J.*, 1955, 2017.

CH *stretching bands* ($cm.^{-1}$) *of methyl ethers and, in square brackets, reference compounds.*

The compounds were examined in CCl_4 solution on a Perkin-Elmer Model 21 double-beam spectrometer fitted with a calcium fluoride prism. Figures in parentheses are molecular extinction coefficients ($mole^{-1}$ l. $cm.^{-1}$) units. No intensity values are given for shoulders (sh) on the sides of main bands. Various compounds (in square brackets) not containing methoxy-groups are included in the Table for reference. The bands are divided into frequency ranges, and each column is designated by a letter as shown.

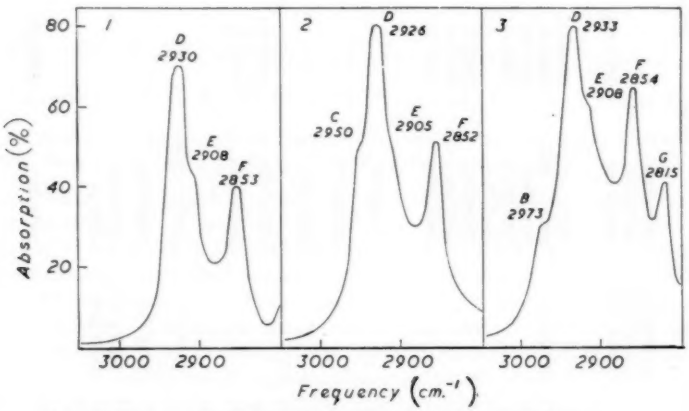
No.	A 3100	B 3000	C 2970	D 2950	E 2920	F 2890, 2880	G 2840	2810
Acyclic compounds								
[1 Di-*n*-butyl ether]			2960(250)	2933(220)		2865(205)		
2 *n*-Hexyl methyl ether		2990 sh	2958(140)	2929(170)		2863(125)	2825(55)	
3 *trans*-Hex-3-en-1-yl methyl ether	3030(20)	2985 sh	2868(110)	2928(110)	2894(90)	2872(95)	2823(60)	
cyclo*Hexane derivatives*								
[4 *cyclo*Hexane]				2930(>275)	2908 sh	2853(180)		
[5 Methyl*cyclo*hexane]			2950 sh	2926(>285)	2905 sh	2852(215)		
6 Methoxy*cyclo*hexane		2973 sh		2933(280)	2908 sh	2854(155)	2815(75)	
7 *trans*-4-Methoxy*cyclo*hexanol		2978 sh		2938(200)	2908 sh	2862(110)	2820(45)	
8 *cis*-4-Methoxy*cyclo*hexanol		2978 sh		2943(210)		2864(100)	2822(45)	
9 4-Methoxy*cyclo*hexanone		2978 sh		2941(120)	2893 sh	2876(70)	2824(45)	
10 *trans*-1 : 4-Dimethoxy*cyclo*hexane		2982(80)		2943(240)	2905 sh	2864(135)	2821(115)	
11 *cis*-1 : 4-Dimethoxy*cyclo*hexane		2980(55)		2943(240)	2905 sh	2864(120)	2819(120)	
cyclo*Hexene derivatives*								
[12 3-Ethoxy*cyclo*hexene]	3034(30)	2982(75)		2944(103)		2870(75) 2846 sh		
13 3-Methoxy*cyclo*hexene	3034(25)	2983 sh		2943(95)		2878 sh 2840 sh	2818(40)	
[14 4-Ethoxy*cyclo*hexene]	3028(25)	2975(75)		2928(95)		2878 sh 2844(65)		
15 4-Methoxy*cyclo*hexene	N.I.	2975(50)		2923(185)	2898 sh	2863 sh 2840(75)	2820(65)	
16 *endo*-4-Methoxy*bicyclo*[2 : 2 : 1]hept-1-ene	3068(25)	2981(145)		2938(105)	2895 sh	2862(55)	2819(35)	
Steroids								
[17 Cholest-5-en-3β-ol]	3028 sh		2958 sh	2938(>385)		2868(275) 2857 sh		
18 3β-Methoxycholest-5-ene	3033 sh		2953 sh	2938(395)		2868(220) 2853 sh	2828(115)	
19 3β-Methoxyergosta-7 : 22-dien-11-one			2958(345)	2933(285)		2868(220)	2820(75)	
20 3β-Methoxyergosta-8 : 22-dien-11-one			2958(410)	2938 sh		2869(265)	2823(90)	
Aromatic compounds								
[21 Phenetole]	3068(15) 3038(20) 2983(60)			2928(30)	2903(30)	2875(30)		
22 Anisole	3068(20) 3033(25) 3000(30)			2948(45)	2908(30)		2832(40)	
23 Veratrole	N.I.			2948(60)	2904(40) 2892 sh		2832(60)	

N.I. = not investigated in this region.

Materials. Nos. 3, 7, 8, 10, 11, 14, 15, and 16: Henbest and Nicholls, unpublished work. 19 and 20, Jones, Meakins, and Stephenson, unpublished work. The remaining compounds were prepared by published methods, or by purification of commercial products.

found in a few series, such as the esters of the long-chain acids,[6] the spectra of most compounds are rendered complex by the occurrence of vibrational coupling, etc. (for an example see the discussion by Plyler and Acquista [2a] of the CH stretching region of *cyclo*hexane and *cyclo*pentane hydrocarbons).

In view of these factors it is impracticable to make rigid assignments of bands A—G. However, it seems possible to associate them for the first 20 compounds with structural features as follows: (A) CH stretching of olefinic groups.[7,8] Antisymmetric CH stretching of (B) CH_3 in OEt and OMe groups; (C) CH_3 in *C*-Me groups; and (D) CH_2 in all types of methylene group. (E) Where present, probably due to CH_2 groups. (F) Symmetric CH stretching of CH_2 in all types of methylene group and CH_3 in *C*-Me and OEt groups.



1, cyclo*Hexane*. 2, *Methyl*cyclo*hexane*. 3, *Methoxy*cyclo*hexane*.

(G) Symmetric CH stretching of CH_3 in OMe groups. This was developed by considering the bands of compounds nos. **4**, **5**, and **6**, and applying the deductions from these to the other examples. Clearly the observed peaks and shoulders are merely the sum totals of many partially overlapping bands: it must be stressed therefore that the specified vibrations are to be regarded as the ***main*** modes, but by no means the only ones, leading to the various bands. The most important correlation, relating band G to the methoxyl group, implies that connection of methyl to oxygen instead of carbon lowers the frequency of the symmetric CH_3 stretching mode by about 50 cm.$^{-1}$. Band B (thought to be associated with methyl in methoxyl and ethoxyl groups) shows a shift in the opposite direction for the antisymmetric methyl vibration: this correlation has been noted previously for ethoxyl groups.[3]

In the aromatic compounds (nos. **21**—**23**) the bands above 3000 cm.$^{-1}$ are due to aromatic CH stretching, and those at 2832 cm.$^{-1}$ (nos. **22** and **23**) are again associated with methoxyl, but more examples are needed for detailed analysis of the spectra.

We are grateful to the Department of Scientific and Industrial Research for a grant (to B. N.) and to Miss W. Peadon for technical assistance.

THE UNIVERSITY, MANCHESTER, 13. [*Received, October 12th*, 1956.]

[6] Sinclair, McKay, Myers, and Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 2578.
[7] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402.
[8] Henbest, Meakins, Nicholls, and Wilson, *J.*, 1957, 997.

282. *The Photolysis of Trifluoroacetaldehyde.*

By R. E. Dodd and J. Watson Smith.

The photolysis of trifluoroacetaldehyde has been studied over a wide range of temperatures and pressures by use of light of wavelength 3130 Å. The products are trifluoromethane, hexafluoroethane, hydrogen, and carbon monoxide. Quantum yields of the first and last up to 60 indicate a chain reaction involving trifluoromethyl radicals produced in the initial step. An alternative primary process yielding trifluoromethane and carbon monoxide directly has a probable quantum efficiency of 0·021. Rate constants are given for the abstraction by trifluoromethyl radicals of hydrogen from trifluoroacetaldehyde, methane, *iso*butane, and acetaldehyde. The association of two trifluoromethyl radicals has been shown not to depend significantly upon total pressure down to 0·5 mm. Side reactions, evident at low temperatures, are discussed.

Photolytic reactions of acetone, azomethane, and acetaldehyde have been extensively studied both for their own interest and to investigate the reactions of methyl radicals. Analogous interest lies in the fluorinated compounds and the photolyses of trifluoroacetone,[1] hexafluoroacetone,[2] and hexafluoroazomethane[3,4] have been reported. The first yields methyl radicals; the course of photolysis of the third is complicated by the addition of trifluoromethyl radicals to the parent compound, and evidently hexafluoroacetone is the best source of trifluoromethyl radicals. We now describe the photolysis of trifluoroacetaldehyde, CF_3·CHO; evidence is given for the participation of trifluoromethyl radicals in a chain reaction, and a rate constant is evaluated for the abstraction of the hydrogen atom from the aldehyde. Figures are given[5] for the rate of abstraction by trifluoromethyl radicals of hydrogen from other compounds and, where there has been duplication, the results agree well with those[4,6] obtained from the use of other radical sources.

Combination of methyl radicals to form ethane requires the presence of a third body[7,8] which, by energy transfer on collision, stabilises the excited ethane molecule first formed. This led us to seek a similar pressure dependence in the combination of trifluoromethyl radicals. Down to pressures of 0·5 mm. of trifluoroacetaldehyde it appears that there are sufficient collisions to sustain the rate of formation of hexafluoroethane at the same value as at higher pressures. A lower limit is given for the mean life of the excited C_2F_6 complex.

Evidence is given for two primary processes, one leading directly to the formation of trifluoromethane and carbon monoxide, the other a dissociation into CF_3· and ·CHO radicals.

As in the photolysis of acetaldehyde, the part played by the formyl radical, ·CHO, is not readily discerned. Quantum yields suggest that at high temperatures its main fate is decomposition with the subsequent appearance of a trifluoromethyl radical; there is little evidence about its fate at low temperatures: a wall reaction is possible. Just as a wall reaction leading to methane has been noticed at low temperatures in the photolysis of acetone and acetaldehyde, so it appears that a similar reaction yields trifluoromethane in addition to its homogeneous production.

[1] Sieger and Calvert, *J. Amer. Chem. Soc.*, 1954, **76**, 5197.
[2] Ayscough and Steacie, *Proc. Roy. Soc.*, 1956, *A*, **234**, 476.
[3] Dacey and Young, *J. Chem. Phys.*, 1955, **23**, 1302.
[4] Pritchard, Pritchard, Schiff, and Trotman-Dickenson, *Trans. Faraday Soc.*, 1956, **52**, 849.
[5] Dodd and Smith, *Research*, 1956, **8**, s63.
[6] Ayscough, Polanyi, and Steacie, *Canad. J. Chem.*, 1955, **33**, 743; Ayscough and Steacie, *ibid.*, 1956, **34**, 106.
[7] Kistiakowsky and Roberts, *J. Chem. Phys.*, 1953, **21**, 1135.
[8] Dodd and Steacie, *Proc. Roy. Soc.*, 1954, *A*, **223**, 283.

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Experimental

The photolysis of gaseous trifluoroacetaldehyde was studied with light predominantly of wavelength 3130 Å. The ranges of pressure, temperature, and intensity of light were respectively 0·5—100 mm., 18—400°, and (0·2—9) $\times$ 10^{-11} einsteins $cm.^{-3}$ $sec.^{-1}$. The two cylindrical reaction vessels (one of Vitreosil, length 8 cm., volume 237 c.c., and the other of Pyrex, length 80 cm., volume 1330 c.c.) were equipped with plane end-windows. Provision was made for the larger reaction system to be further increased in volume, for pressures below 2 mm., by including a 3 l. bulb through which the contents were circulated by a mercury-vapour pump. The vessels were electrically heated and the temperature was maintained within 1° along their lengths. Pressures were measured by a constant-volume mercury manometer, a magnifying manometer (mercury and dibutyl phthalate, magnification about $\times$10), and a McLeod gauge. Reaction times varied from a few minutes to 48 hr.

The light source was a British Thomson-Houston ME/D 250 w high-pressure mercury arc. Aqueous potassium chromate was used as a filter. A Pyrex plate was used as an additional filter in front of the Vitreosil vessel. The ultraviolet absorption spectrum of trifluoroacetaldehyde begins at about 3500 Å and rises to a broad maximum at about 3020 Å (ε 5·8 at 3020 and 5·3 at 3130 Å in hexane) with a second region of strong absorption commencing at 2450 Å. From the absorption spectrum of the aldehyde, the known transmission of the filters, and the measured output of the lamp it was estimated that virtually all the absorption took place in the reaction system between 2900 and 3400 Å, with 80% in the range 3070 to 3200 Å.

Light was collected either by a quartz flask filled with water or (for most of the work) by a large polished aluminium reflector giving a slightly converging beam. The illuminated volumes were taken to be equal to the volumes of the reaction vessels, not including side-arms. Relative light intensities were measured with an EEL selenium cell (screened by Chance OX7 filter glass and a filter solution of nickel and cobalt sulphates) whose area was sufficient to receive most of the light passing through the vessel. The amount of light absorbed was calculated, with corrections for reflection from the rear windows of the vessel and the furnace, from the transmitted intensity by interpolation in a Beer's-law graph. Calibration was made against the quantum yield of carbon monoxide formation ($\Phi_{CO} = 1·0$) in the photolysis of acetone vapour at 125°. The calibration was frequently checked and was revised whenever the system was adjusted. Relative to the standard the accuracy of measurement was of the order of $\pm$5%.

Materials.—Trifluoroacetaldehyde was prepared from trifluoroacetic acid by Rosenmund reduction of the acid chloride,[9] in the preparation of which [10] it was found best to maintain the mixture of the acid and benzoyl chloride at 60° until most of the acid chloride had been evolved (about 1 hr.) and then to raise the temperature to 150°, instead of raising the temperature gradually during 24 hr. The acid chloride was condensed and allowed to evaporate (20 g. in 2—3 hr.) into a stream of hydrogen (10 l. per hr.), which carried it over the reducing palladised-asbestos catalyst. This was maintained at 230°; use of this temperature prevented production of the tar obtained at the temperature (250°) used by Brown and Musgrave.[9] To prevent production of hydrate the cylinder hydrogen was passed through palladised asbestos at 250° to remove oxygen, and thence through a trap cooled in liquid air. The colourless solid product, evidently polymeric, was warmed to 50° with a few drops of concentrated sulphuric acid and low-temperature fractionation of the evolved gas demonstrated the presence of hydrogen chloride. A subsequent fraction which distilled at 0·5 mm. at $-130°$ was monomeric trifluoroacetaldehyde (b. p. $-20°$) which could now be condensed and kept without danger of polymerisation. That some polymerisation occurred on the inner surface of the apparatus at room temperature was evident from the formation of white feathery crystals of hydrate whenever leakage admitted moist air. Molecular-weight measurements and the infrared spectrum (identical with that published by Husted and Albrecht [11]) showed the sample to be substantially pure.

The mass spectrum of the aldehyde (Table 1) showed the expected peaks, including that corresponding to the $CF_3{\cdot}CHO^+$ ion and two rearrangement peaks at mass numbers 32 and 51. The latter is of unusual magnitude, but the absence of other unaccountable peaks and the constant

[9] Brown and Musgrave, *J.*, 1952, 5049.
[10] Henne, Alm, and Smook, *J. Amer. Chem. Soc.*, 1948, **70**, 1968.
[11] Husted and Albrecht, *ibid.*, 1952, **74**, 5420.

relative intensity of the peak at mass number 51 convinced us that it could not be due to impurity in the aldehyde.

Methane (from a cylinder) was passed over active copper at 200°, condensed at −196°, and,

TABLE 1. *Mass spectrum of trifluoroacetaldehyde.*

m/e	Ion	Peak height (cm.)	*m/e*	Ion	Peak height (cm.)	*m/e*	Ion	Peak height (cm.)
19	F	1·0	31	CF	52·0	63	CF_2·CH	3·5
20	HF	2·0	32	CFH	18·5	69	CF_3	80·8
24	C_2	1·1	43	C_2F	2·5	78	CF_2·CO	5·7
25	C_2H	1·0	44	C_2FH	4·8	79	CF_2·CHO	14·0
28	CO	36·1	50	CF_2	128·0	82	CF_3·CH	2·2
29	CHO	414·0	51	CF_2H	240·0	98	CF_3·CHO	34·4

after pumping, distilled at −184°. After several distillations mass-spectrometric analysis showed a satisfactory purity.

*iso*Butane (98% pure) was subjected to trap-to-trap distillation between −130° and −196°.

Acetaldehyde was distilled from anhydrous calcium sulphate at 21° and then at low temperature *in vacuo*.

Trifluoromethane and hexafluoroethane (kindly supplied by Imperial Chemical Industries Limited, General Chemicals Division) were used to calibrate the mass spectrometer and were first roughly fractionated and then distilled at −160°/0·5 mm.

Analysis of Products.—Systematic analysis was made for carbon monoxide, hydrogen, trifluoromethane, and hexafluoroethane: these were separated by low-temperature fractionation, the fractions being measured by a combined Toepler pump and gas-burette. The non-condensable gases, carbon monoxide and hydrogen, were measured and then oxidised on copper oxide, the carbon monoxide being measured as dioxide. In experiments with added methane analysis of the non-condensable gases by this means was not feasible. Trifluoromethane and hexafluoroethane could not be separated since their vapour-pressure curves practically coincide; they formed the two constituents of a fraction taken off at −160° and relative proportions were then assessed by mass-spectrometry or infrared absorption. A mass-spectral analysis based on peaks 51 for trifluoromethane and 119 for hexafluoroethane was complicated by the fact that the sensitivity at the peak 119 was affected by the presence of trifluoromethane. Hexafluoroethane was therefore estimated from the residual peak at mass 69 after subtraction of the contribution from trifluoromethane. Reproduciblity to within 0·5% was obtained for normal mixtures but when the ratio $CF_2H : C_2F_6$ became as high as 30 : 1 the errors in mass-spectral analysis became large. Infrared absorption for trifluoromethane based on bands at 1250 cm.$^{-1}$ for hexafluoroethane and 1150 cm.$^{-1}$ for trifluoromethane was used satisfactorily for such mixtures.[12]

When ethane was expected among the products, small amounts could be detected in the fluorocarbon fraction as a difference between the total pressure and the combined partial pressures, measured spectrophotometrically, of trifluoromethane and hexafluoroethane. Mass-spectral examination of the products was made for carbon tetrafluoride, silicon tetrafluoride, and also for possible fluorocarbons of higher molecular weight.

Rates of production (mole cm.$^{-3}$ sec.$^{-1}$) are referred to as follows: carbon monoxide, R_{CO}; hydrogen, R_H; trifluoromethane, R_M; hexafluoroethane, R_E. Intensity of light absorbed, I_a, was measured in einsteins cm.$^{-3}$ sec.$^{-1}$.

RESULTS AND DISCUSSION

Photolysis above 150°.—Preliminary experiments indicated a reaction considerably slower than the photolysis of acetaldehyde under the same conditions. Non-condensable products were entirely carbon monoxide and small quantities of hydrogen. The only condensable products which could be identified were trifluoromethane and hexafluoroethane: their presence was first indicated by vapour-density measurements and was confirmed and their concentration estimated by their mass and infrared spectra.

[12] Ayscough, *Canad. J. Chem.*, 1955, **33**, 1566.

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Insignificant traces of silicon tetrafluoride were occasionally detected by mass spectometry : there was no real evidence of thermal decomposition or attack on Pyrex glass or silica at temperatures up to 400°.

Quantum yields as high as 60 indicated a chain reaction and the rate of formation of carbon monoxide was proportional to the square-root of the light intensity. This and the nature of the products suggested a reaction mechanism similar to that for acetaldehyde, *viz.* :

$$CF_3{\cdot}CHO + h\nu \longrightarrow CF_3{\cdot} + {\cdot}CHO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$CF_3{\cdot} + CF_3{\cdot}CHO \longrightarrow CF_3{\cdot}CO{\cdot} + CF_3H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$CF_3{\cdot}CO{\cdot} \longrightarrow CF_3{\cdot} + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$CF_3{\cdot} + CF_3{\cdot} \longrightarrow C_2F_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

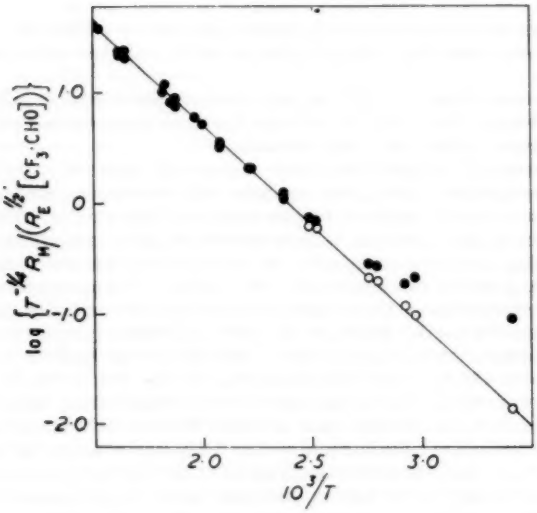

FIG. 1. *Dependence of* $R_M/R_E^{\frac{1}{2}}[CF_3{\cdot}CHO]$ *on temperature.*

●, uncorrected values.

Fluorine-abstraction reactions such as :

$$CF_3{\cdot} + CF_3{\cdot}CHO \longrightarrow CF_4 + {\cdot}CF_2{\cdot}CHO$$

or

$$CF_3{\cdot} + CF_3{\cdot} \longrightarrow CF_4 + CF_2{\cdot}$$

were discounted by the absence of carbon tetrafluoride, in agreement with similar findings with trifluoroacetone, hexafluoroacetone, and hexafluoroazomethane.

If reactions (2) and (4) are the sole contributors to the rates of formation of trifluoromethane and hexafluoroethane, then

$$\rho = R_M/(R_E^{\frac{1}{2}}[CF_3{\cdot}CHO]) = k_2/k_4^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (i)$$

should be independent of light intensity and of aldehyde pressure and should conform to a linear Arrhenius plot of $\log_{10} \rho T^{-\frac{1}{2}}$ against $1/T$. At 262° and about 50 mm. pressure the values of ρ were 41·7 and 41·0 $mole^{-\frac{1}{2}}$ $cm.^{\frac{3}{2}}$ $sec.^{-\frac{1}{2}}$ for absorbed intensities $3{\cdot}22 \times 10^{-11}$ and $2{\cdot}2 \times 10^{-12}$ einsteins $cm.^{-3}$ $sec.^{-1}$, *i.e.*, a fourteen-fold intensity variation. At the same temperature, pressures of 9, 50, and 90 mm. gave values of ρ of 40·8, 41·2, and 41·1. Although below 150° there was some variation with pressure and a marked variation with intensity these figures agree with the above assumptions at the stated temperature. The

Arrhenius plot is shown in Fig. 1 and it is clear that there is linearity above 150°. The line corresponds to

$$k_2/k_4^{\frac{1}{2}} = (1{\cdot}95 \times 10^4)T^{\frac{1}{2}} \exp(-8200/RT)$$

Thus $E_2 - \frac{1}{2}E_4 = 8{\cdot}2 \pm 0{\cdot}5$ kcal./mole and, collision diameters 5·7 and 4·0 Å for $CF_3{\cdot}CHO$ and CF_3 respectively being assumed, the ratio of the probability factors $P_2/P_4^{\frac{1}{2}} = 5{\cdot}3 \times 10^{-3}$. Ayscough [13] has shown that $E_4 < 1{\cdot}5$ kcal./mole and that $P_4 = 0{\cdot}16$ if $E_4 = 0$. Hence E_2 is close to 8·2 kcal./mole and P_4 to $2{\cdot}1 \times 10^{-3}$.

Abstraction of Hydrogen by Trifluoromethyl Radicals.—Photolysis of trifluoroacetaldehyde in the presence of compounds containing hydrogen, *viz.*, methane, *iso*butane, and acetaldehyde, gave a higher proportion of trifluoromethane in the products, clearly owing to an additional reaction

$$CF_3{\cdot} + RH \longrightarrow CF_3H + R{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2')$$

and consequently

$$\rho = R_M/(R_E^{\frac{1}{2}}[CF_3{\cdot}CHO]) = k_2/k_4^{\frac{1}{2}} + k_{2'}[RH]/(k_4^{\frac{1}{2}}[CF_3{\cdot}CHO]) \quad . \quad . \quad (ii)$$

Knowledge of $k_2/k_4^{\frac{1}{2}}$ allowed $k_{2'}/k_4^{\frac{1}{2}}$ to be deduced from the measurements of ρ in the presence of appropriate amounts of RH. Fig. 2 shows the Arrhenius plots for $k_{2'}/k_4^{\frac{1}{2}}$ for the compounds cited: the curves correspond to $k_{2'}/k_4^{\frac{1}{2}} = 1{\cdot}96 \times 10^4 T^{\frac{1}{2}} \exp(-10{,}400/RT)$ for methane, $5{\cdot}4 \times 10^3 T^{\frac{1}{2}} \exp(-4500/RT)$ for *iso*butane, and $2{\cdot}5 \times 10^3 T^{\frac{1}{2}} \exp(-4000/RT)$ for acetaldehyde. The values of $E_{2'} - \frac{1}{2}E_4$ and of $P_{2'}/P_4^{\frac{1}{2}}$ have already been reported.[5] The excellent agreement between our values of $k_{2'}$ for methane and *iso*butane and those derived for the same compounds in experiments with hexafluoroacetone as the source of trifluoromethyl radicals [6] is valuable confirmation of our interpretation of the linear portion of Fig. 1.

In discussing the reaction of methyl radicals with tetrafluoroethylene, Danby and Raal [14] have postulated a reaction (2″) in which the trifluoromethyl radical induces the decomposition of acetaldehyde without itself suffering any change:

$$CF_3{\cdot} + CH_3{\cdot}CHO \longrightarrow CF_3{\cdot} + CH_4 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2'')$$

Their data indicate that $1{\cdot}41(k_{2''}/k_4^{\frac{1}{2}})(k_\beta^{\frac{1}{2}}/k_\alpha) = 12{\cdot}8$ (the ratio of their constants C''/C') where k_α and k_β refer to the reactions

$$CH_3{\cdot} + CH_3{\cdot}CHO \longrightarrow CH_4 + CH_3{\cdot}CO{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (\alpha)$$

$$CH_3{\cdot} + CH_3{\cdot} \longrightarrow C_2H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (\beta)$$

$k_\alpha/k_\beta^{\frac{1}{2}}$ has been measured [15] and has a probable value at 300° of 191 mole$^{-\frac{1}{2}}$ cm.$^{\frac{3}{2}}$ sec.$^{-\frac{1}{2}}$. Hence $k_{2''}/k_4^{\frac{1}{2}}$ would be $0{\cdot}707 \times 12{\cdot}8 \times 191 = 1730$ mole$^{-\frac{1}{2}}$ cm.$^{\frac{3}{2}}$ sec.$^{-\frac{1}{2}}$, which is four times faster than the hydrogen-abstraction reaction (2′) between trifluoromethyl radicals and acetaldehyde which we have measured ($k_{2'}/k_4^{\frac{1}{2}} = 427$ at 300°). Unfortunately we did not analyse the non-condensable gases in our experiments with acetaldehyde, and therefore lack evidence on the occurrence of reaction (2″), which would produce four times as much methane as the extra trifluoromethane given by (2′). Nor is it clear that inclusion of reaction (2′) would significantly affect Danby and Raal's interpretation of their results (except to increase the complexity of the theoretical expressions) although they state that their experimental results require no loss of fluoromethyl radicals. They did not analyse for trifluoromethane.

Pressure-dependence of Trifluoromethyl Radical Combination.—If the combination of trifluoromethyl radicals required third-body collisions for deactivation of the active $C_2F_6^*$

[13] Ayscough, *J. Chem. Phys.*, 1956, **24**, 944.
[14] Danby and Raal, *J.*, 1950, 1596.
[15] Volman and Brinton, *J. Chem. Phys.*, 1952, **20**, 1764; Ausloos and Steacie, *Canad. J. Chem.*, 1955, **33**, 31; Dodd, *ibid.*, 1955, **33**, 699.

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complex there should be a pressure below which collisions are insufficiently frequent to sustain the rate constant $k_4 = R_E/[CF_3\cdot]^2$ at its high-pressure value. Consequently ρ should begin to increase as the aldehyde pressure is decreased and should show the form of dependence upon pressure which has been found [8] at low pressures in the photodecomposition of acetone where the recombination of methyl radicals is similarly involved. Experiments at 124° gave values of ρ which rose from 3·5 at high pressures to between 7 and 8 at 1 mm. When it later became apparent that a correction had to be applied, as discussed below, the corrected values, though showing a rather large spread at the low pressures, gave no indication of a trend to higher values. Eight corrected values between 0·75 and

FIG. 2. *Abstraction of hydrogen by trifluoromethyl radicals from* (a) isobutane, (b) *acetaldehyde, and* (c) *methane.*

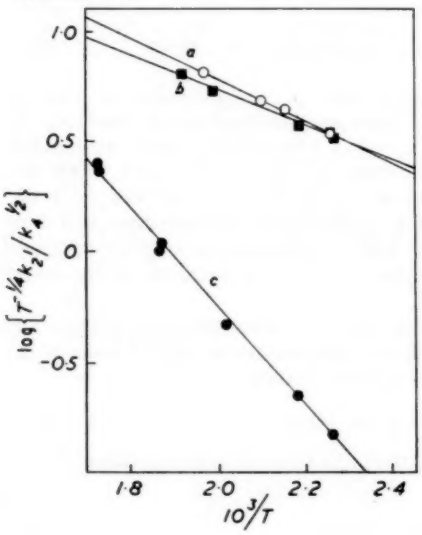
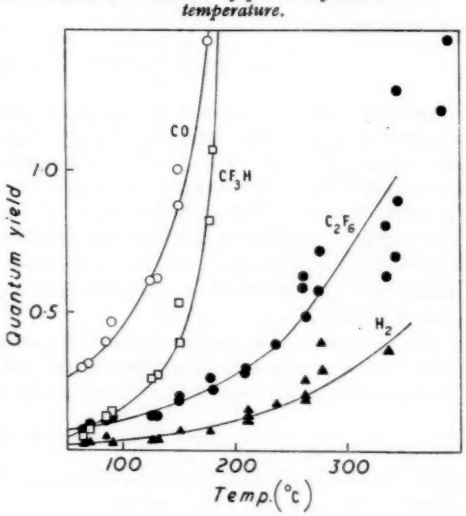


FIG. 3. *Variation of quantum yields with temperature.*



7·5 mm. averaged 3·2 ± 0·7 and ten between 7·5 and 25 mm. averaged 2·9 ± 0·1. At 209°, where the correction is negligible, values were found as in Table 2.

TABLE 2. *Pressure variation at* 209°.

$CF_3\cdot CHO$ (mm.)...	42	30	27	8·9	6·9	3·1	2·4	1·1	0·5
ρ	16·2	16·6	17·2	17·5	19·9	19·3	19·2	19·3	19·7

A slight increase in ρ can be seen but not the appreciable increase found for methyl radicals at 0·5 mm. of acetone. There is thus no real evidence of dependence upon pressure down to 0·5 mm. of aldehyde. The data of Table 2 imply that the unimolecular rate constant for decomposition of the active $C_2F_6^*$ complex at 209° is less than $3{\cdot}3 \times 10^6$ sec.$^{-1}$, or that the mean life of the complex is greater than 3×10^{-7} sec. This may be compared with the lower limit of $1{\cdot}6 \times 10^{-8}$ sec. estimated [8] for the active $C_2H_6^*$ complex at 247°. It is plausible to suppose that the longer lifetime of the $C_2F_6^*$ complex is related to the fact that in hexafluoroethane all other vibrational levels lie close to or below that involving predominantly the stretching of the carbon–carbon bond. The accumulation of critical energy in that mode is therefore less likely than it is in the case of hexafluoroethane where a larger number of the other vibrational levels lie above that attributed to C–C stretching.

Quantum Yields.—The quantum yields of carbon monoxide, trifluoromethane, hexafluoroethane, and hydrogen at various temperatures are shown in Fig. 3. These were determined in the same experiments as recorded in Fig. 1, mainly at about the same pressure of aldehyde (30—40 mm.) and at intensities in the range (1·6—5) $\times$ 10^{-11} einsteins cm.$^{-3}$ sec.$^{-1}$. Quantum yields at the room temperature at various intensities are given in Table 3.

TABLE 3. *Quantum yields at room temperature.*

$I_a \times 10^{11}$	8·66	3·94	1·45	0·57	0·55	0·44	0·155
CO	0·18	0·17	0·18	0·20	0·19	0·19	0·23
CF_3H	0·030	0·033	0·040	0·055	0·057	0·064	0·073
C_2F_6	0·060	0·054	0·055	0·055	0·055	0·062	0·064
H_2	0·016	0·019	0·013	—	0·016	0·014	0·018

The yields, Φ_E, of hexafluoroethane are of particular interest. It is not clear why the spread of the values should be so great above 250° and we are not prepared to defend the three values greater than unity. There is, however, sufficient evidence that $\Phi_E > \frac{1}{2}$ above about 250°, although the sequence of reactions (1)—(4) requires that $\Phi_E = k_1 \leqslant 0{\cdot}5$. There is evidently a further source of trifluoromethyl radicals and reactions (5) and (6) are suggested.

$$\cdot CHO \longrightarrow H\cdot + CO \quad . . . . . (5)$$

$$H\cdot + CF_3\cdot CHO \longrightarrow H_2 + CF_3\cdot CO\cdot \quad . . . . . (6)$$

If reactions (5), (6), and (3), respectively, are the only fates of the species ·CHO, H·, and CF_3·CO·, then $\Phi_E = k_1 \leqslant 1$. Thus k_1 is probably close to unity above 350°. The quantum yield of hydrogen, Φ_H, should then be equal to Φ_E but we were not able to measure this with even moderate accuracy above about 280°.

At lower temperatures Φ_E would be expected to fall to half its value at high temperatures, since reaction (5), which strongly depends upon temperature ($E_5 = 14$—15 kcal./mole), will be replaced by an alternative reaction for formyl radicals: for example, the wall reaction postulated by Calvert and Steacie [16] as occurring in the photolysis of formaldehyde. The observed value, 0·06, of Φ_E at room temperature implies not only that reactions (5) and (6) no longer participate, but that either k_1 is itself small ($= 2\Phi_E =$ 0·12) at 20° or trifluoromethyl radicals are consumed in reactions other than (4). We were able to detect at about 4465 Å some fluorescence arising from irradiation of the aldehyde at 3130 Å. This implies that $k_1 < 1$; but there is also evidence discussed below for other reactions in which trifluoromethyl radicals are lost.

The deviation from linearity which can be seen in Fig. 1 at temperatures below 150° is an indication of a significant contribution to R_M from a reaction other than (2) and less dependent upon temperature. Such would be a primary intramolecular rearrangement, as is also probable in the photolysis of acetaldehyde, *viz.*:

$$CF_3\cdot CHO + h\nu \longrightarrow CF_3H + CO \quad . . . . . (1')$$

This would naturally imply that $k_1 \leqslant 1$. It would also require that ρ be proportional to intensity, or that:

$$\Phi_M = R_M/I_a = (k_2/k_4^{\frac{1}{2}})R_E^{\frac{1}{2}}[CF_3\cdot CHO]/I_a + k_{1'} \quad . . . . . (iii)$$

Hence a plot of R_M/I_a against $R_E^{\frac{1}{2}}[CF_3\cdot CHO]/I_a$ should give a straight line of slope $k_2/k_4^{\frac{1}{2}}$ and intercept $k_{1'}$. The results in Table 3 have been tested in this way (Fig. 4, curve *A*). Equation (iii) is apparently obeyed, the intercept having the value $k_{1'} = 0{\cdot}021$. On the other hand the slope (0·148) is greater than the value (0·063) of $k_2/k_4^{\frac{1}{2}}$ which is obtained by extrapolation from the linear portion of Fig. 1. Curve *C* represents equation (iii) with $k_2/k_4^{\frac{1}{2}} = 0{\cdot}063$. The quantity $\Phi_M - (k/k_4^{\frac{1}{2}})R_E^{\frac{1}{2}}[CF_3\cdot CHO]/I_a$ should be constant ($= k_{1'}$)

[16] Calvert and Steacie, *J. Chem. Phys.*, 1951, **19**, 176.

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but in Fig. 4, curve *B*, is shown to be proportional to $R_E^{\frac{1}{2}}[CF_3{\cdot}CHO]/I_a$. The earlier discussion has demonstrated that reaction (4) is the only significant source of hexfluoroethane at higher temperatures : it is unlikely that it should not be so at lower temperatures and therefore $R_E^{\frac{1}{2}}$ is a measure of the concentration of trifluoromethyl radicals. Thus there is implied a third reaction leading to trifluoromethane whose rate is proportional to

$$CF_3{\cdot} + {\cdot}CHO \longrightarrow CF_3H + CO \quad . . . . . \quad (7)$$

$${\cdot}CHO + CF_3{\cdot}CHO \longrightarrow CF_3H + CO + {\cdot}CHO \quad . . . . . \quad (8)$$

$[CF_3]$. (The dependence on aldehyde pressure was not examined, for all the experiments were performed at one pressure.) Reactions such as (7) and (8) do not explain this

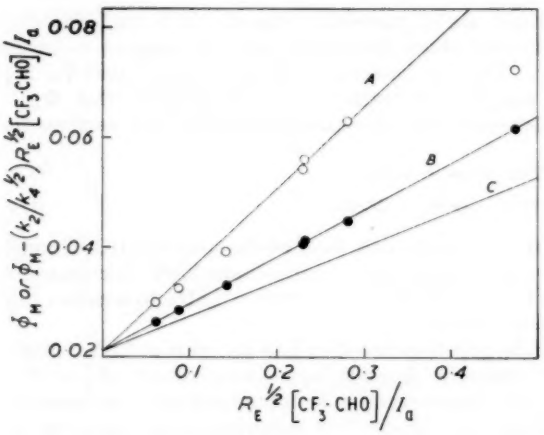

FIG. 4. *Dependence of quantum yield of trifluoromethane upon intensity.*

A, eqn. (iii), slope 0·148.
B, eqn. (iv), slope 0·085.
C, eqn. (iii), slope 0·063.

proportionality, which suggests a reaction (9) between trifluoromethyl radicals and aldehyde adsorbed on the walls of the vessel :

$$CF_3{\cdot} + CF_3{\cdot}CHO\ (wall) \longrightarrow CF_3H + products \quad . . . . . \quad (9)$$

Equation (iii) then becomes :

$$\Phi_M - (k_2/k_4^{\frac{1}{2}})R_E^{\frac{1}{2}}[CF_3{\cdot}CHO]/I_a = k_{1'} + \{k_9/(k_4^{\frac{1}{2}}[CF_3{\cdot}CHO])\} \times \{R_E^{\frac{1}{2}}[CF_3{\cdot}CHO]/I_a\} \quad (iv)$$

The slope (0·085) of curve *B* in Fig. 4, the aldehyde concentration ($2{\cdot}33 \times 10^{-6}$ mole cm.$^{-3}$), and the value of k_4 ($2{\cdot}34 \times 10^{13}$ mole^{-1} cm.^{3} sec.$^{-1}$ [13]) permit a calculation of $k_9 = 0{\cdot}96$ sec.$^{-1}$. This can be compared with the value, 422 sec.$^{-1}$, obtained if every trifluoromethyl radical were to react at every collision with the wall (geometrical area 154 cm.^{2}) in a volume of 237 cm.^{3}. Defined as $R_M/[CF_3{\cdot}]$ for reaction (9), k_9 includes the fraction of surface occupied by adsorbed aldehyde as well as the likelihood of reaction of a radical with an adsorbed aldehyde molecule. The ratio $0{\cdot}96/422 = 2{\cdot}3 \times 10^{-3}$ therefore seems entirely reasonable. At increased temperatures a decrease in the fraction adsorbed and an increase in the reaction rate would act in opposition and thus k_9 should be more or less independent of temperature. Above 20° the deviations in ρ were not measured with sufficient accuracy to allow reliable estimates of k_9. That the deviations vary little with temperature and become relatively unimportant above 150° is shown by applying the above value of k_9 (obtained at room temperature) as a correction [by use of equation (iv)] to all the points in Fig. 1 below 150°. The open points thus obtained lie well on the extrapolated Arrhenius line for $k_2/k_4^{\frac{1}{2}}$.

The wall reaction (9) provides an alternative fate for trifluoromethyl radicals which would reduce Φ_E at room temperature: its effect is small. Thus, in a typical experiment ($I_a = 1{\cdot}45$ in Table 3) the contributions to Φ_M from reactions (1'), (2), and (9) are respectively 0·021, 0·008, and 0·011 and hence $\Phi_E = \frac{1}{2}(k_1 - 0{\cdot}011) = 0{\cdot}055$. k_1 is thus estimated to be 0·12, but the term arising from (9) is small as is necessary to agree with the fact that Φ_E does not vary significantly with intensity. On this interpretation we should expect the quantum yield of carbon monoxide, arising from reactions (1'), (3), and probably (9), to be greater than Φ_M by an amount (not greater than k_1) which depends upon the fate of the ·CHO radicals. The results from the same experiment thus give $k_1 \geqslant 0{\cdot}18 - 0{\cdot}04 = 0{\cdot}14$. Since k_1 obtained from Φ_E has about the same value, it is implied that the major contribution to Φ_{CO} is from the formyl radicals all of which must appear as carbon monoxide. Moreover, since $\Phi_H = 0{\cdot}016$ (average), they must do so by a reaction path such that only a fifth of them yield molecular hydrogen. It is not clear how this may be.

Similar reasoning applied to other reactions which might be suggested for the low value of Φ_E does not lead to any greater value of k_1. Thus if it is assumed that reaction (3) does not occur at low temperatures but that (10) does, the value of k_1 obtained for Φ_E is 0·13. The effect of (10) is no greater because the yield of $CF_3{\cdot}CO{\cdot}$ radicals is only equal to the

$$CF_3{\cdot} + CF_3{\cdot}CO \longrightarrow CF_3{\cdot}CO{\cdot}CF_3 \quad \ldots\ldots\ldots\ldots \quad (10)$$

contribution, 0·008, of reaction (2) to Φ_M. Ayscough and Steacie[2] give some evidence for the immediate decomposition of any trifluoroacetyl radicals which may be formed photolytically from hexafluoroacetone. Reaction (10) is evidently not required to explain our present results. No evidence could be found for hexafluoroacetone, which would be produced in (10), on mass-spectrometric examination of the higher-boiling products.

The above arguments based upon material balance show that the yields of carbon monoxide agree with those of trifluoromethane and hexafluoroethane but that the apparent efficiency of the primary split is low. We did not study the effect of inert gases on quantum yield and there is insufficient evidence to show whether a relatively stable activated complex, $CF_3{\cdot}CHO^*$, is responsible for a low value of k_1 or whether there is a considerable degree of recombination between trifluoromethyl and formyl radicals.

We are indebted to Dr. W. K. R. Musgrave for a sample of trifluoroacetaldehyde and advice on its preparation; to Mr. P. Kelly for mass-spectrometric measurements, and to King's College (University of Durham) and the Ministry of Education for maintenance awards.

KING'S COLLEGE, NEWCASTLE UPON TYNE, 1. [*Received, October 18th*, 1956.]

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283. *The Thermal Decomposition of Nitrous Oxide. The Effect of Foreign Molecules.*

By T. N. Bell, P. L. Robinson, and A. B. Trenwith.

The kinetics of the decomposition of nitrous oxide in the presence of carbon dioxide, carbon tetrafluoride, and the inert gases have been studied over the temperature range 650—750° and with pressures of nitrous oxide of 50—100 mm., and compared with results obtained with sulphur dioxide.[1] For these conditions the empirical rate equation is:

$$\text{Rate} = k'[N_2O]^{1\cdot55} + k''[N_2O]^{0\cdot55}[X]$$

Decomposition of the nitrous oxide molecule follows its activation by the two processes

$$N_2O + N_2O \longrightarrow N_2O^* + N_2O\ ;\quad N_2O + X \longrightarrow N_2O^* + X$$

The activation energy of the second of these is about 3 kcal. higher than that of the first. The efficiencies of the various foreign gases have been compared by determining the several ratios of the rate constants of the above reactions. From these results the relative efficiencies " collision per collision " have been calculated. The results indicate a behaviour of the inert gases different from that displayed by them in other unimolecular decompositions.

In studying the oxidation of sulphur dioxide by nitrous oxide [1] we found that the sulphur dioxide participates in the formation of activated nitrous oxide molecules which are produced by the reactions

$$N_2O + N_2O \underset{(1')}{\overset{(1)}{\rightleftharpoons}} N_2O^* + N_2O;\quad N_2O + SO_2 \underset{(2')}{\overset{(2)}{\rightleftharpoons}} N_2O^* + SO_2$$

Experiment indicates that reaction (2′) is less likely to occur than (1′) since there is no noticeable fall-off in the initial rate of reaction as the concentration of sulphur dioxide is increased, the graphs of initial rate against sulphur dioxide concentration being straight lines over the pressure range studied. We observed an energy difference, $E_2 - E_1$, of approximately 14 kcal.; this magnitude was difficult to understand, but, owing to the scatter of the points on one of the Arrhenius plots the figure was uncertain.

In order to test the reality of this energy difference we investigated the decomposition of nitrous oxide in the presence of carbon dioxide which accelerates the decomposition of nitrous oxide without undergoing chemical change.[2] Although the efficiency of reaction (2) compared with that of (1) for the nitrous oxide–carbon dioxide system had been estimated,[3] no data were available for comparing the activation energies of the two steps. This system has the advantage over the nitrous oxide–sulphur dioxide system that it can be followed by change of pressure with time, thus giving more accurate figures for initial rates. (The sulphur dioxide reaction, involving no change in pressure, must be followed by the tedious and less accurate method of gas analysis.) With carbon dioxide present we found that E_2 was greater than E_1 by approximately 3 kcal. An energy difference of the same order appeared when the added gas was carbon tetrafluoride.

Besides enabling us to compare the activation energies of reactions (1) and (2), the results afforded a method of comparing the efficiencies of the reactions. In the case of carbon dioxide, our relative efficiency figure differs appreciably from that of Volmer, Kummerow, and Nagasako,[2,3] whose results have been criticised on several grounds by Lindars and Hinshelwood.[4] Their experiments were not done at sufficiently high pressures

[1] Bell, Robinson, and Trenwith, *J.*, 1955, 1440.
[2] Volmer and Kummerow, *Z. phys. Chem.*, 1930, **9**, *B*, 141.
[3] Nagasako, *ibid.*, 1931, **11**, *B*, 420; Volmer and Frohlich, *ibid.*, 1932, **19**, *B*, 85; Volmer and Bogdan, *ibid.*, 1933, **21**, *B*, 257.
[4] Lindars and Hinshelwood, *Proc. Roy. Soc.*, 1955, *A*, 231, 162.

to give an accurate value for k_∞, the limiting value of the first-order rate constant for the decomposition of nitrous oxide from which the relative efficiencies were calculated. The inaccuracies are apparent when their figures for k_∞ are compared with those calculated from the relation $k_\infty = 10^{11.7} \exp(-61{,}000/RT)$ derived by Hunter [5] from measurements at very high pressures.

Although carbon tetrafluoride accelerates the decomposition of nitrous oxide,[4] data on its relative efficiency were not available. We have found it to be the most effective of the foreign gases studied, being almost as efficient as nitrous oxide itself.

Published values of relative efficiencies of the inert gases in unimolecular reactions show them generally to increase with atomic weight. For the decomposition of nitrous oxide the only figures available are those of Volmer *et al.* which indicate that the relative efficiencies of the inert elements decrease in order of increasing atomic weight. To check this departure from the usual influence of the inert gases, their effect on the rate of decomposition of nitrous oxide has been studied, and their several relative efficiencies have been determined. Our figures for these, although different from those of Volmer *et al.*, show the same trend for the first four members, namely a decrease with increase in atomic weight. Xenon is singular in that its efficiency is approximately the same as that of argon.

Experimental

Materials.—(i) Nitrous oxide (anæsthesia grade) was dried (P_2O_5) and fractionated between $-130°$ and $-196°$, head and tail fractions being rejected. Before use it was repeatedly frozen and evaporated, occluded non-condensable gases being pumped off. The purified gas was stored in a 3 l. bulb. (ii) Carbon tetrafluoride from a cylinder (Imperial Chemical Industries) was dried (P_2O_5) and condensed in a trap cooled in liquid nitrogen; occluded non-condensable gases were pumped off, and the gas was distilled in a low-temperature Podbielniak-type column. A middle cut of the fraction boiling at $-129°$ was collected and stored in a 3 l. bulb. (iii) Carbon dioxide was obtained by allowing "Drikold" to evaporate in an evacuated bulb. The gas was condensed in a trap cooled in liquid nitrogen and then fractionated at $-130°$ into another trap cooled in liquid nitrogen, a middle cut being retained. After another similar fractionation the gas was deemed sufficiently pure. (iv) Helium, neon, argon, krypton, and xenon were transferred from the soda-glass containers in which they were supplied by the British Oxygen Company to a sampling bulb on the apparatus. Mass spectrometry showed the specimens to contain 99·99% of the gas in question with the exception of argon, which carried 0·2% of air, and xenon, which had 0·3% of krypton.

Apparatus.—A cylindrical reaction vessel, 15 cm. × 4·5 cm., of clear silica was used. It had a thermocouple well and capillary inlet and was connected to the rest of the system, which was of Pyrex glass, by a ground cone-and-socket joint sealed with Picein wax. The whole was evacuated by a mercury diffusion pump backed by a rotary oil pump. The reaction vessel was heated in a well-lagged tubular furnace the temperature of which was kept within $\pm 1°$ of that required by means of a "Sunvic" energy regulator and hot-wire switch. Temperatures were measured with a chromel–alumel thermocouple in conjunction with a "Doran" potentiometer. A constant volume manometer [6] was used to measure the pressure. The use of two cathetometers, one fixed and focused on the constant head and the other movable and focused on the moving limb of the manometer, gave improved accuracy. The reaction vessel was connected through a two-way tap to two sampling bulbs, dead space being kept to a minimum.

Operation.—The reactants were introduced separately into the reaction vessel, the time interval between successive additions being less than 5 sec. Pressure–time readings were taken during the first 10 to 15 min. at approximately half-minute intervals. Before every run the reaction vessel was kept under vacuum for 15 min.

Results and Discussion

A series of estimations of initial rates of reaction were made for mixtures with the same initial nitrous oxide concentration and various amounts of carbon dioxide, and also with the same initial carbon dioxide concentration and various amounts of nitrous oxide.

[5] Johnston, *J. Chem. Phys.*, 1951, **19**, 663.
[6] Dodd and Robinson, "Experimental Inorganic Chemistry," Elsevier, Amsterdam, 1954, 122.

The plots of initial rate against the varied concentrations (Figs. 1 and 2) yield the following empirical rate equation for the decomposition of nitrous oxide in the presence of the added gas:

$$\text{Rate} = k'[N_2O]^x + k''[N_2O]^y[X]$$

where [X] is the concentration of the foreign gas. This equation corresponds to that

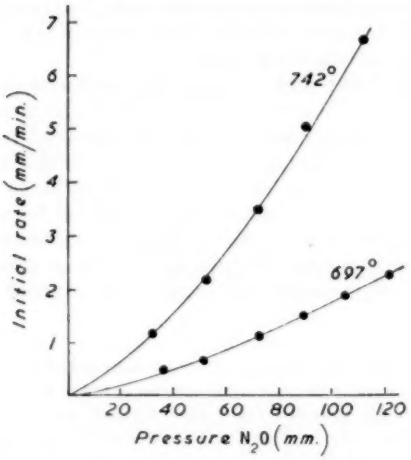

FIG. 1. *Variation of initial rate with pressure of nitrous oxide.*

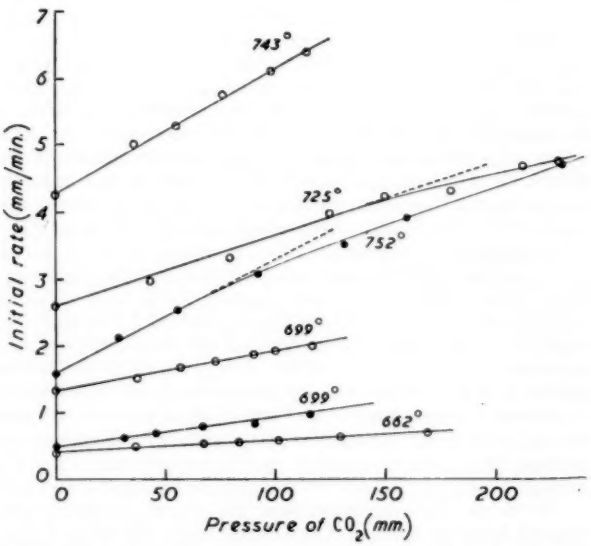

FIG. 2. *Variation of initial rate with pressure of carbon dioxide.*

● N_2O pressure = 50 mm.
○ N_2O pressure = 100 mm.

given for the nitrous oxide–sulphur dioxide system, the initial rate curves being similar.[1]

In general, the above equation holds only when [X] is less than $[N_2O]$, for when the concentration of the added gas exceeds that of the nitrous oxide the points on the initial rate–[X] curve for constant nitrous oxide concentration deviate negatively from the straight line (Fig. 2).

Values of x were obtained from the plots of initial rate of reaction against [X] for the specific concentrations of 50 mm. and 100 mm. of nitrous oxide, measurements being made at 699° and 743°. x can be determined from the ratio of the intercepts at a particular

temperature since these correspond to $k'[N_2O]^x$. The slopes of the graphs correspond to $k''[N_2O]^y$, so that y can be determined from their ratio. This assumed that x and y do not vary with pressure, which, though not strictly true, introduces a negligible error since the order of the nitrous oxide decomposition is known to change very little over our pressure range.

TABLE 1.

Added gas	Temp.	x	y	Added gas	Temp.	x	y
Carbon dioxide	699°	1·45	0·51	Carbon tetrafluoride ...	701°	1·60	0·62
,, ...	743	1·54	0·51	,, ...	730	1·61	0·57

Similar experiments with carbon tetrafluoride as the added gas were made at 701° and 730°. The values for x and y are summarised in Table 1, giving means of 1·55 and 0·55 respectively.

The empirical rate equation for pressures of nitrous oxide between 50 and 100 mm. is thus:

$$\text{Rate} = k'[N_2O]^{1\cdot55} + k''[N_2O]^{0\cdot55}[X].$$

In accounting for our results we have adopted the following simple mechanism for the decomposition of nitrous oxide in the presence of a foreign gas:

$$N_2O + N_2O \underset{(1')}{\overset{(1)}{\rightleftharpoons}} N_2O^* + N_2O \qquad O + N_2O \xrightarrow{(4)} O_2 + N_2$$

$$N_2O + X \underset{(2')}{\overset{(2)}{\rightleftharpoons}} N_2O^* + X \qquad O + N_2O \xrightarrow{(5)} 2NO$$

$$N_2O^* \xrightarrow{(3)} N_2 + O \qquad O \xrightarrow{(6)} \text{Walls}$$

Steps (4), (5), and (6) have recently been suggested by Kaufman, Gerri, and Bowman [7] as representing the most probable fates of atomic oxygen. They considered the reaction $O + O + M \longrightarrow O_2 + M$ improbable on the grounds that it involves triple collisions and that the presence of an inert gas is unlikely to increase this probability since such atoms are known to be remarkably inefficient third bodies.

Steps (1)—(6) lead to the theoretical rate equation

$$\text{Rate} = \frac{k_1[N_2O]^2 + k_2[N_2O][X]}{1 + k_{1'}[N_2O]/k_3 + k_{2'}[X]/k_3}\left\{\frac{2k_4[N_2O] + 2k_5[N_2O] + k_6}{k_4[N_2O] + k_5[N_2O] + k_6}\right\}$$

For small additions of the foreign gas the rate, as indicated by the straight lines in Fig. 2, depends on the first power of the concentration of the foreign gas. Thus the term $k_{2'}[X]/k_3$ must be small when [X] is small. Neglecting this term we have

$$\text{Rate} = \frac{k_1[N_2O]^2}{1 + k_{1'}[N_2O]/k_3}\left\{\frac{2k_4[N_2O] + 2k_5[N_2O] + k_6}{k_4[N_2O] + k_5[N_2O] + k_6}\right\} + \frac{k_2[N_2O][X]}{1 + k_{1'}[N_2O]/k_3}\left\{\frac{2k_4[N_2O] + 2k_5[N_2O] + k_6}{k_4[N_2O] + k_5[N_2O] + k_6}\right\}$$

The first term corresponds to that which would be obtained for the decomposition of nitrous oxide alone and can be identified with the first term of our empirical equation. The experimental order of 1·55 agrees with that calculated from the results of Lewis and Hinshelwood [8] for the pressure 50—100 mm. and 652°. As can be gathered from the theoretical rate equation, $x - y$ should equal unity, as is found experimentally. The mechanism postulated thus yields a theoretical equation similar in form to the empirical

[7] Kaufman, Gerri, and Bowman, *J. Chem. Phys.*, 1956, **25**, 106.
[8] Lewis and Hinshelwood, *Proc. Roy. Soc.*, 1938, *A*, **168**, 441.

equation. Hence the theoretical equation may be assumed to apply within the limited pressure range studied. We realise, however, that for a wider pressure range it would be necessary to invoke the more elaborate theoretical treatments of other authors.

In graphs such as those in Fig. 2, the expression Slope × $[N_2O]$/Intercept corresponds to k''/k', which equals k_2/k_1 in the theoretical rate equation. To determine this ratio a series of experiments were made at several temperatures with fixed initial concentrations of nitrous oxide. The results in Table 2 were derived from the slopes and intercepts of the plots of initial rate against pressure of the foreign gas. We judge the values of k_2/k_1 to have an accuracy of ±5%.

TABLE 2.

Carbon dioxide present						Carbon tetrafluoride present					
N_2O (mm.)	Temp.	k_2/k_1	N_2O (mm.)	Temp.	k_2/k_1	N_2O (mm.)	Temp.	k_2/k_1	N_2O (mm.)	Temp.	k_2/k_1
100	651°	0·42	100	725°	0·47	100	673°	0·80	50	730°	0·90
100	662	0·42	50	743	0·47	105	690	0·84	100	730	0·88
100	679	0·46	100	743	0·46	55	701	0·82	50	744	0·91
50	699	0·44	50	752	0·49	105	701	0·83			
100	699	0·46									

Plots of log (k_2/k_1) against $1/T$ gave for ΔE $(= E_2 - E_1)$ values of 2·3 and 3·6 kcal. with carbon dioxide and carbon tetrafluoride respectively. All the energy values quoted, except those for the sulphur dioxide reaction, have been derived from the Arrhenius plots by the method of least squares. In addition, values were obtained for $k' = \text{Intercept}/[N_2O]^{1.55}$ and $k'' = \text{Slope}/[N_2O]^{0.55}$. The Arrhenius plots for the individual rate constants gave with carbon dioxide: E', 53·6; E'', 55·9; $E'' - E'$, 2·3; and with carbon tetrafluoride 54·0, 57·6, and 3·6 kcal. respectively. As we found in the oxidation of sulphur dioxide, the values for E' are close to the accepted figure for the energy of activation of the decomposition of nitrous oxide itself. The agreement between ΔE and $E'' - E'$ provides a satisfactory check for the individual results.

To round off the work on the decomposition of nitrous oxide in the presence of sulphur dioxide, values for k_2/k_1 were calculated and $\log(k_2/k_1)$ plotted against $1/T$. The results are given in Table 3.

TABLE 3.

N_2O (mm.)	100	100	200	100	100
Temp.	652°	678°	678°	708°	736°
k_2/k_1	0·54	0·54	0·53	0·62	0·74

ΔE may be between 5 and 10 kcal.; it could not be precisely fixed from the Arrhenius plot owing to the scatter of the points.

The fraction k_2/k_1 is a measure of the relative efficiency of the foreign gas in activating the nitrous oxide, and from it can be derived the more useful quantity ρ, the relative efficiency " collision per collision," defined as the ratio of N_2O–N_2O collisions to N_2O–X collisions causing the same rate of formation of activated nitrous oxide molecules. According to the kinetic collision theory

$$\rho = \frac{k_2}{k_1}\left\{\frac{2\sigma(N_2O)}{\sigma(X) + \sigma(N_2O)}\right\}^2\left\{\frac{2M(X)}{M(N_2O) + M(X)}\right\}^{\frac{1}{2}}$$

where σ (Y) and M(Y) are the respective kinetic collision diameters and molecular weights of the species Y. Unfortunately there are no generally accepted values for collision diameters which can be used in calculating kinetic results. The published figures vary considerably, depending on their mode of calculation. We have used those given by Rowlinson,[9] who, for spherically symmetrical molecules such as carbon tetrafluoride

[9] Rowlinson, *Quart. Rev.*, 1954, **8**, 168.

and the inert gases, took σ as the mean of the values calculated from viscosity data and from the second virial coefficients, and for the remaining molecules calculated σ for the critical volumes. The collision diameters used here are as follows: He, 2·6; Ne, 2·8; A, 3·4; Kr, 3·6; Xe, 4·0; CF_4, 4·7; CO_2, 3·7; SO_2, 4·0; N_2O, 3·7 Å.

Calculations show that for both carbon dioxide and sulphur dioxide ρ is about equal to k_2/k_1 and for carbon tetrafluoride is $0{\cdot}8961k_2/k_1$. Thus ρ for carbon dioxide varies between 0·42 and 0·49 over our temperature range. This value was so different from that (1·3) of Volmer *et al.* as to lead us to determine by the same procedure the efficiency " collision per collision " of the inert gases.

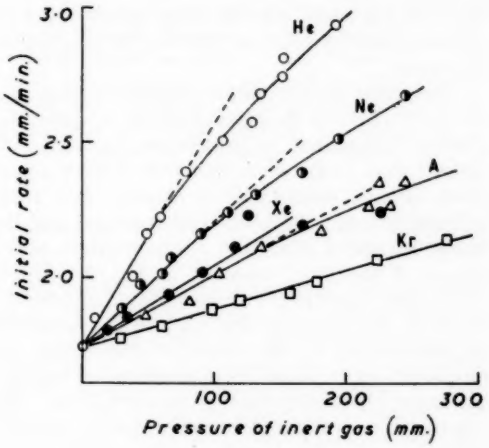

FIG. 3. *The influence of the inert gases on the initial rate of reaction.*

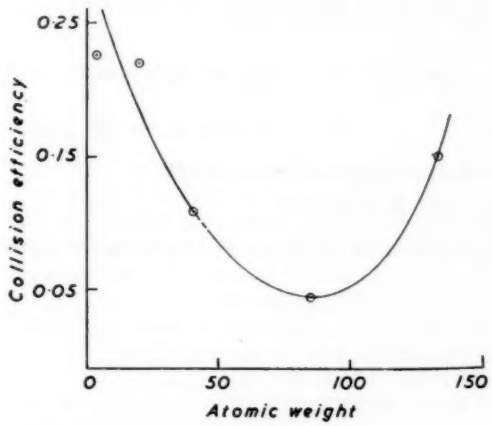

FIG. 4. *Variation of the collision efficiency of the inert gases with atomic weight.*

Initial rates were measured in the presence of different quantities of the several inert gases. Throughout the temperature was 708° and the pressure of nitrous oxide 98·8 mm. The graphs of initial rate against inert gas concentration, shown in Fig. 3, allowed values for k_2/k_1, which we believe to have an accuracy of $\pm 0{\cdot}004$, to be obtained from the intercepts and the slopes of the straight portions. The results for k_2/k_1, with the calculated collision efficiencies, are: He, 0·488 (0·275); Ne, 0·261 (0·268); A, 0·149 (0·158); Kr, 0·079 (0·094); Xe, 0·176 (0·199).

Fig. 4 shows the plot of ρ against the atomic weight of the inert gas.

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The results indicate that the quantity ΔE is real, though of the order of only a few kcal. As the production of an activated nitrous oxide molecule, which will subsequently split according to reaction (3), does not appear to be a simple process, this small difference in activation energy seems reasonable. As a result of the difference, the collision efficiencies of the inert gases become temperature-dependent. Whether this phenomenon is general cannot yet be decided, as the reliable data on collision efficiencies in the literature refer to one temperature only.

Of particular interest are the values found for the relative efficiencies of the inert gases. Although the actual values differ appreciably from those of Volmer *et al.*[3] they show a similar decrease with increase in atomic weight as far as krypton, but xenon reverses the trend, being more efficient than either argon or krypton. The earlier workers found xenon to have a collision efficiency of 0·16 as compared with 0·18 for krypton and 0·20 for argon.

The trend of the relative efficiency figures in Table 5 bears no resemblance to those of the inert gases as displayed in other unimolecular decompositions where a fairly regular increase with atomic weight has been found.[10,11,12,13] For example, Volpe and Johnston[13] showed that, in the decomposition of nitryl chloride, the relative efficiencies of the inert gases increase approximately linearly with their boiling points, and with the force of collision between the individual inert gas and the reactant molecule (the latter quantity being calculated from the Lennard-Jones potential). Using our results, we obtained curves of the form depicted in Fig. 4. We conclude, therefore, that the behaviour of the inert gases in the decomposition of nitrous oxide is exceptional since the differences to which we refer seem too large to be accounted for by either experimental error or the approximations of the simplified theoretical treatment. It is of interest that recent ultrasonic experiments[14] on mixtures of nitrous oxide and helium and of nitrous oxide and argon show that the number of N_2O–A collisions necessary to dissipate a vibrational quantum is approximately ten times the number of N_2O–He collisions required for the same purpose. The higher efficiency of helium in this process may bear some relation to its greater effect in promoting the decomposition of nitrous oxide.

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KING'S COLLEGE, NEWCASTLE UPON TYNE, 1. [*Received, October 18th*, 1956.]

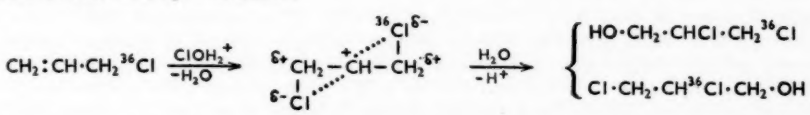
[10] Pritchard, Sowden, and Trotman-Dickenson, *Proc. Roy. Soc.*, 1953, *A*, **217**, 563.
[11] *Idem, ibid.*, 1953, *A*, **218**, 416.
[12] Wilson and Johnston, *J. Amer. Chem. Soc.*, 1953, **75**, 5763.
[13] Volpe and Johnston, *ibid.*, 1956, **78**, 3903.
[14] Walker, Rossing, and Legvold, Natl. Advisory Comm. for Aeronautics, Technical Note 3210, 1954.

284. *The Kinetics and Mechanisms of Addition to Olefinic Substances. Part IV.* Rearrangement accompanying Addition of Hypochlorous Acid to 3-Chloro-2-methylpropene.*

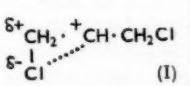
By P. Ballinger and P. B. D. de la Mare.

The addition of hypochlorous acid to 3-chloro-2-methylpropene in water, under catalysis by perchloric acid, gives 1 : 3-dichloro-2-methylpropan-2-ol (94 pts.) and 2 : 3-dichloro-2-methylpropanol (6 pts.). By labelling the 3-chlorine atom in the starting material, and examining the specific activity of 1-chloro-2 : 3-epoxy-2-methylpropane derived from the latter product, it has been shown that 38% of the 2-chlorine atoms in the 2 : 3-dichloro-2-methylpropanol were attached to the 3-carbon atom in the starting material. This result is discussed in terms of the properties of the carbonium ion, which is presumed to be intermediate in the above addition. 2 : 3-Dichloro-2-methylpropanol and αβ-dichloro-α-methylpropionic acid have been characterised for the first time.

Carbonium ions, , are generally considered to be intermediates in the addition of hypochlorous acid to unsaturated compounds, and stereochemical evidence exists to show that the entering electrophilic chlorine atom can interact, electrostatically or otherwise, with the adjacent carbonium ionic centre. In certain cases, the reactions of such intermediates can be studied by using isotopic tracers. Thus, if hypochlorous acid is added to 3-[^{36}Cl]chloropropene, some of the product is the unsymmetrical dichlorohydrin, 2 : 3-dichloropropanol; and if this is partly or wholly derived from an intermediate symmetrical about the 2-carbon atom, then ^{36}Cl will be found in the 2-position, to an extent which is a measure of reaction by this route.



In fact, study of this addition has shown that only about 12% of the unsymmetrical dichlorohydrin is derived through such a symmetrical intermediate. In principle, the remainder might conceivably have been derived by attack of the electrophilic reagent at the 2-carbon atom to give the carbonium ion, $^{+}CH_2{\cdot}CHCl{\cdot}CH_2{}^{36}Cl$. It was argued, however, that this was not the main intermediate concerned, since other electrophilic reagents (*e.g.*, HCl, HOH) add to 3-chloropropene to give the product in which the electrophilic part of the addendum (in these cases, H) is attached to the 1-carbon atom. Instead, it was considered that there is produced first the intermediate (I), which then reacts so rapidly with solvent molecules that the chlorine atoms in the carbonium ion do not have time to become completely equivalent.



(I)

If this interpretation is correct, then attachment of electron-releasing groups in the 2-position should stabilise the carbonium ion and allow it to last for a longer time before reaction with the solvent. In this way, reaction through the symmetrical intermediate should be favoured. To test this prediction, the addition has now been examined of hypochlorous acid to 3-chloro-2-methylpropene. In this case, the unsymmetrical chlorohydrin, 2 : 3-dichloro-2-methylpropanol, which must be examined to test the proposed theory, is expected to be formed in relatively small amount, since the 2-methyl group will

* Part III, *J.*, 1956, 3337.

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certainly divert the orientation towards the formation of the symmetrical chlorohydrin, 1 : 3-dichloro-2-methylpropan-2-ol. The latter compound is known [1,2] to be the main product of the addition of chlorine water, or of hypochlorous acid, to 3-chloro-2-methylpropene, and the by-products known in this reaction [2] are those olefinic materials which could be formed by elimination of a proton from the carbonium ion, $CH_2Cl{\cdot}^+CMe{\cdot}CH_2Cl$, followed by addition to these olefinic substances.

Experimental

Some of the materials and general methods have been described in previous papers.[3] Commercial 3-chloro-2-methylpropene (which contains *ca.* 4% of the isomeric 1-chloro-2-methylpropene, b. p. 69°) was dried and fractionated, the first 10%, which distilled below 72°, being discarded. The major fraction was refractionated with a high reflux ratio and the first 10% being again discarded; the product had b. p. 72·0—72·2°/756 mm., n_D^{25} 1·4250. To label this material with ^{36}Cl, the 3-chloro-2-methylpropene (95 g.) was refluxed for two days with acetone and $Li^{36}Cl$, prepared from $H^{36}Cl$ (3·0 ml. of 1·6N; specific activity 114 μc per g. of Cl; supplied by the Radiochemical Centre, Amersham). The product was washed repeatedly with water to remove acetone and lithium chloride, dried, and fractionated, and had b. p. 72°, n_D^{25} 1·4250.

1 : 3-Dichloro-2-methylpropan-2-ol, prepared from 1 : 3-dichloroacetone and methylmagnesium bromide,[4] had b. p. 63°/12 mm., n_D^{24} 1·4730 (Found: C, 33·5; H, 5·6; Cl, 49·1. Calc. for $C_4H_8OCl_2$: C, 33·6; H, 5·6; Cl, 49·7%). Its reaction with aqueous alkali is very rapid even at 0°, but a rough estimate of the second-order rate coefficient, over the last 5% of the reaction, is k_2 (0·0°) = *ca.* 10^2 l. mole^{-1} min.$^{-1}$.

Preparation of 2 : 3-*Dichloro-2-methylpropanol.*—Methacrylic acid (127 g.) was added slowly to a stirred solution of chlorine in carbon tetrachloride (*ca.* 1 l.) containing a trace of stannic chloride. More chlorine was introduced, and the whole was cooled at *ca.* −80° until the gas ceased to be absorbed. After removal of solvent, the product gave, on fractionation, *αβ-dichloro-α-methylpropionic acid* (160 g.), b. p. 110°/4 mm., n_D^{25} 1·4670, d_4^{25} 1·3629, m. p. 23—24° (Found: C, 30·5; H, 3·9. $C_4H_6O_2Cl_2$ requires C, 30·6; H, 3·8%). Its *S-benzylthiuronium salt* had m. p. 140° (Found: C, 45·2; H, 5·4; N, 8·8; Cl, 22·3; S, 10·0. $C_{12}H_{16}O_2N_2Cl_2S$ requires C, 44·6; H, 5·0; N, 8·7; Cl, 22·0; S, 9·9%). The dichloro-acid (136 g.) was then refluxed for 5 hr. with redistilled thionyl chloride (167 g.). Excess of thionyl chloride was removed, and the product gave on fractionation the acid chloride (98 g.), b. p. 46·5°/11·5 mm., 160°/770 mm., n_D^{24} 1·4670. An ethereal solution of this (98 g.) was added to a stirred suspension of lithium aluminium hydride (18 g.) in ether; then the excess of reagent was decomposed with water, and the ether solution poured into ice and 6N-sulphuric acid. The ether layer was removed, and the aqueous solution was again extracted with ether. The combined ether-extracts were washed with sodium hydrogen carbonate solution, then with water, and dried ($MgSO_4$). Fractionation of the residue gave 2 : 3-*dichloro-2-methylpropanol* (58 g.), b. p. 70°/9 mm., 180°/760 mm. (slight decomp.), n_D^{25} 1·4746, d_4^{25} 1·2680 (Found: C, 33·8; H, 5·7; Cl, 49·6. $C_4H_8OCl_2$ requires C, 33·6; H, 5·6; Cl, 49·7%). The 3 : 5-dinitrobenzoate, prepared in the absence of bases, had m. p. 104°.

Kinetics of the Reaction of 2 : 3-*Dichloro-2-methylpropanol with Aqueous Sodium Hydroxide.*—2 : 3-Dichloro-2-methylpropanol reacts with alkali to give, in good yield, 1-chloro-2 : 3-epoxy-2-methylpropane, as is shown below. It has been presumed that there are no side reactions which significantly affect the measured kinetic form, since titration of a solution containing a known weight of the starting material, after reaction with a known excess of alkali to completion of the reaction of which the kinetic form is measured, gives a result which corresponds, within experimental error, with the release of one mole of hydrogen chloride from one mole of dichlorohydrin. A subsidiary experiment showed that 1-chloro-2 : 3-epoxy-2-methylpropane reacts with alkali under the chosen experimental conditions at a rate which is negligibly slow in comparison with the rate of liberation of the first mole of hydrogen chloride from the dichlorohydrin.

The following is an example of a typical run, in which the chlorohydrin (0·0255M) was allowed to react at 24·9° with 0·0725N-sodium hydroxide. Samples (5·0 ml.) were withdrawn at intervals, quenched in acetone containing 0·0801N-hydrochloric acid (5·46 ml.) and back-titrated with 0·00889N-ethanolic potassium hydroxide, with lacmoid as indicator.

Time (min.)	0·0	0·71	1·49	5·25	8·19	13·51	27·21	∞
Titre (ml.)	8·47	10·20	11·46	16·28	19·00	20·56	22·34	22·88
k_2 (l. mole^{-1} min.$^{-1}$)	—	2·54	2·24	2·31	2·64	2·34	2·25	—

Mean k_2 = 2·39 l. mole^{-1} min.$^{-1}$.

The values for the second-order rate constants are calculated by means of the expression $k_2 = 2{\cdot}303[\log_{10} b(a - x)/a(b - x)]/t(a - b)$, where the symbols have their usual significance. The zero of time is that of mixing of the reactants, and hence the absence of any appreciable rapid initial reaction shows the absence of the fast-reacting 1 : 3-isomer. When the latter is present, a plot of x against time (t) gives a curve, substantially straight near the beginning, which by extrapolation to $t = 0$ gives an estimate of the amount of the faster-reacting isomer in the mixture, since practically all the 1 : 3-isomer has reacted before the first point is taken. Trial determinations by this method with artificial mixtures of the two isomers in known proportion were accurate to ±2 units %.

When equimolecular proportions of the reactants (both 0·0500M) were taken, the mean value of k_2 for pure 2 : 3-dichloro-2-methylpropanol was found to be 2·79 l. mole^{-1} min.$^{-1}$.* Mixtures of the isomers were sometimes assayed in this way, by using the graph of $1/(a - x)$ against t as described previously.[3]

Reaction of Hypochlorous Acid with 3-Chloro-2-methylpropene.—Experiment (i). 3-Chloro-2-methylpropene (71 g.) was dissolved in an aqueous solution (*ca.* 80 l. in a 100 l.-flask) of silver perchlorate (0·02M) and perchloric acid (0·02M), kept at 25° ± 2° by the use of a glass-shielded immersion heater. To the stirred solution was added hypochlorous acid (in total, 3·5 l., 0·166M) at such a rate that the concentration of hypochlorous acid in the reaction mixture was always below 0·001M. On completion of the reaction, the mixture was saturated with ether (6 l.), then with sodium chloride (30 kg.). The ether layer was removed and the aqueous solution was extracted with ether (2 × 4 l.). The ether extracts were dried ($MgSO_4$). After removal of the ether, there were obtained fractions: (*a*) 6·2 g., b. p. 27—58°/11 mm., (*b*) 32·5 g. (48%, based on the HOCl taken), b. p. 58·0—60·5°/11 mm., n_D^{25} 1·4725 (Found: C, 33·7; H, 5·7. Calc. for $C_4H_8OCl_2$: C, 33·6; H, 5·6%), (*c*) 3·0 g., b. p. 41—43°/2 mm. The residue from still-pot and column were redistilled, giving (*d*) 1·2 g., b. p. 100—112°/23 mm., and (*e*) tar, 2·9 g. Kinetic analysis showed that fraction (*b*) was nearly pure 1 : 3-dichloro-2-methylpropan-2-ol, whereas fraction (*c*) contained 60% of the latter material and 39% of the isomeric 2 : 3-dichloro-2-methylpropanol. Fractions (*d*) and (*e*) were shown similarly to contain 43% and 34% of the 2 : 3-isomer, together with 34% and 19% of the 1 : 3-isomer respectively, the remainder of each fraction being relatively unreactive with alkali. In order to trace any 2 : 3-isomer in fraction (*b*), 25 g. were dissolved in water (1 l.) and allowed to react for 3 min. at 0° with 2·04N-sodium hydroxide (69 ml., sufficient to hydrolyse 80% of the dichloro-2-methylpropanol). The mixture was extracted with ether and the extract was dried ($MgSO_4$) and fractionated. After removal of ether and 1-chloro-2 : 3-epoxy-2-methylpropane, there were recovered 4·0 g. of the expected 5·0 g. of undecomposed dichloro-2-methylpropanol, b. p. 51·5°/9 mm., n_D^{25} 1·4720. Kinetic analysis revealed the presence of *ca.* 18% of 2 : 3-dichloro-2-methylpropanol; fraction (*b*) thus contained *ca.* 3% of the latter substance. From these determinations, it was possible to assign an approximate value (6—7%) to the proportion of 2 : 3-dichloro-2-methylpropanol recovered from the reaction between hypochlorous acid and 3-chloro-2-methylpropene.

Experiment (ii). 3-[^{36}Cl]Chloro-2-methylpropene (40 ml.) was added in 5 ml. portions to a stirred aqueous solution (*ca.* 8 l. in a blackened vessel) of silver perchlorate (0·02M) and perchloric acid (0·02M), in a thermostat at 24·9°. To this was added 0·211M-hypochlorous acid (in total, 1·92 l.) at such a rate that the concentration of hypochlorous acid in the reaction mixture never exceeded 0·001M. Further measured quantities of silver perchlorate and perchloric acid were added at intervals to keep their concentration at the initial value. On

* The difference between this value and that recorded above probably should be associated with the variation in second-order rate coefficients with concentration of alkali, attributed [5] to the formation, in bulk, of the intermediate alkoxide.

[1] Suter and Malkemus, *J. Amer. Chem. Soc.*, 1941, **63**, 980; Hurd and Abernethy, *ibid.*, p. 976.
[2] Burgin, Hearne, and Rust, *Ind. Eng. Chem.*, 1941, **33**, 386.
[3] de la Mare and Pritchard, *J.*, 1954, 3910, 3990.
[4] Gibson, Harley-Mason, Litherland, and Mann, *J.*, 1942, 171.
[5] Twigg, Wise, Lichtenstein, and Philpotts, *Trans. Faraday Soc.*, 1952, **48**, 699.

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completion of the reaction, the mixture was saturated with ether, then with anhydrous sodium sulphate. The ether layer was removed, the aqueous portion was extracted with ether ($3 \times 1{\cdot}3$ l.), and the ether extracts were dried ($MgSO_4$) and fractionated. After removal of the ether, the crude material was evaporated at 3 mm. pressure into a series of three traps, cooled in ice, carbon dioxide–ethanol, and liquid nitrogen, respectively. The liquid in the ice-trap (40·1 g., 69% based on the hypochlorous acid taken) proved on fractionation to be almost exclusively a mixture of the isomeric dichlorohydrins produced in the reaction. To this was added pure inactive 2 : 3-dichloro-2-methylpropanol (8·377 g.), and the mixture was fractionated. The following fractions were obtained: (*a*) 2·7 g., b. p. 49—52°/8 mm., n_D^{25} 1·4705, (*b*) 28·1 g., b. p. 52·3—52·5°/8 mm., n_D^{25} 1·4724, (*c*) 7·2 g., b. p. 52·5—64·5°/8 mm., and (*d*) 8·45 g., b. p. 64·5—65·0°/8 mm., n_D^{25} 1·4745.

Kinetic analysis of these fractions showed that fraction (*a*) contained 82% of 1 : 3-dichloro-2-methylpropan-2-ol (instantaneous reaction with alkali), with 18% of a substance having $k_2 = ca.$ 47 l. mole^{-1} min.$^{-1}$; fraction (*b*) was nearly pure 1 : 3-dichloro-2-methylpropan-2-ol (Found: C, 33·3; H, 5·6%); fraction (*c*) contained 29·1% of 2 : 3-dichloro-2-methylpropanol ($k_2 = 2{\cdot}74$ l. mole^{-1} min.$^{-1}$); and fraction (*d*) contained 97% of the latter isomer, $k_2 = 2{\cdot}73$ l. mole^{-1} min.$^{-1}$.

A sample of the original 3-chloro-2-methylpropene was hydrolysed with aqueous sodium hydroxide at 60°. The solution was just acidified (sulphuric acid), evaporated to dryness, and ignited. The products were dissolved in water, the solution was filtered, and the total chloride determined (Volhard). Known weights of the other samples were dissolved in water, and their radioactivities determined by the technique usual for liquid samples. The results of radioactive measurements on these samples are shown in Table 1. From these the specific activity of the pure diluted 2 : 3-dichloro-2-methylpropanol is estimated as 1020. From this, and the

TABLE 1. *Radioactive measurements on samples from the reaction of hypochlorous acid with labelled 3-chloro-2-methylpropene.*

Sample	Composition	Concn. (M)	Counts/min.[a]	Spec. activity[b]
1	NaCl from $^{36}Cl{\cdot}CH_2{\cdot}CMe{:}CH_2$	0·05357	244·5	4562 ± 40
2	1 : 3-Dichloro-2-methylpropan-2-ol [fraction (*b*)]	0·1010	458·4	4538 ± 30
3	Mixed dichlorohydrins [fraction (*c*); 29·1% of 2 : 3-dichloro-2-methylpropanol]	0·1015	357·8	3537 ± 18
4	2 : 3-Dichloro-2-methylpropanol, 96·9% [fraction (*d*)]	0·1017	115·3	1137 ± 10

[a] Counts are corrected for background (*ca.* 10/min.). [b] Specific activity is defined here arbitrarily as counts per min. calc. for a M-solution for a particular G.M. tube used for all the measurements. The probable errors are calculated on the basis of random fluctuations in the rate of counting.

weight : dilution ratio of the chlorohydrin mixture obtained from the reaction (40·1 g. of chlorohydrin mixture with 8·377 g. of inactive 2 : 3-dichloro-2-methylpropanol), it is estimated that the percentage of 2 : 3-dichloro-2-methylpropanol in the mixture obtained from the addition reaction was 6·0%, in good agreement with the result of experiment (i).

Fraction (*d*) (6·904 g.) was diluted with pure inactive specimens of 2 : 3-dichloro-2-methylpropanol (9·344 g.) and 1 : 3-dichloro-2-methylpropan-2-ol (1·895 g.) and refractionated; 12·2 g., b. p. 65—67°/9 mm., were collected. Kinetic analysis showed the continued presence of the diluted 1 : 3-isomer, and this was removed as follows. The mixture (11·3 g.) was hydrolysed in water (150 ml.) at 27° for 2 min. with 0·1N-sodium hydroxide (80 ml., sufficient to destroy 10% of the mixture). It was then extracted with ether, and the ether extract was dried and fractionated. After removal of the ether a fraction (7·7 g.) having b. p. 57°/7 mm. was obtained. Kinetic analysis then revealed, within the experimental error (*ca.* 0·5 unit %), no 1 : 3-dichloro-2-methylpropan-2-ol.

This material was diluted again with pure inactive material to give a sample of pure 2 : 3-dichloro-2-methylpropanol (specific activity, 160·3). The mixture (18·1 g.), in water (600 ml.), was hydrolysed completely to the epoxide with 1·58N-sodium hydroxide (81 ml.) at 27° for 30 min., then saturated with ether, and the ether was salted out with anhydrous sodium sulphate. The aqueous layer was kept for counting (sample 8), and the ether extracts were dried and fractionated. There were obtained 10·1 g. (80% yield), b. p. 121·5—122·5°, together with small quantities of unchanged 2 : 3-dichloro-2-methylpropanol (1·1 g.), b. p. 61°/8 mm.,

and material of higher b. p. (*ca.* 0·5 g.). Refractionation gave pure 1-chloro-2 : 3-epoxy-2-methylpropane (4·2 g.), b. p. 122·5°/766 mm., n_D^{25} 1·4308 (cf. ref. 6) (Found : C, 45·1; H, 6·7. Calc. for C_4H_7OCl : C, 45·1; H, 6·6%).

Known weights of the diluted 2 : 3-dichloro-2-methylpropanol and of the derived epoxide were dissolved in ethanol, and their specific activities were determined. As an additional check, these two samples, after counting, were hydrolysed completely by refluxing with excess of 4·5N-sodium hydroxide for 8 hr. The products were just acidified with sulphuric acid, evaporated to dryness, and fused in a silica crucible.

The aqueous layer from the bulk hydrolysis of 2 : 3-dichloro-2-methylpropanol was just acidified with sulphuric acid, and the volatile material was evaporated under a high vacuum. The residue was ignited. Each of the three ignited samples was dissolved in water and filtered. The specific activities of these samples were measured (see Table 2).

TABLE 2. *Radioactive measurements on* 2 : 3-*dichloro-2-methylpropanol and* 1-*chloro-2* : 3-*epoxy-2-methylpropane.*

Sample	Material	Solvent	Concn.	Count/min.[a]	Spec. activity [b]
1	2 : 3-Dichloro-2-methylpropanol	EtOH	1·901	304·9	160·3 ± 1·3
2	1-Chloro-2 : 3-epoxy-2-methylpropane from sample 1	EtOH	2·857	371·2	129·9 ± 1·0
3	Total chloride from sample 1	H_2O [c]	1·752	113·3	129·4 [d] ± 1·7
4	Total chloride from sample 2	H_2O	1·802	189·3	105·1 ± 1·2
5	Chloride from partial hydrolysis of sample 1 ...	H_2O	0·953	28·1	29·5 ± 0·5

[a, b] See footnotes to Table 1. [c] Solutions of compounds containing ^{36}Cl in ethanol and water give counts differing approximately in the ratio 1·24 : 1. [d] After correction for the fact that 2 : 3-dichloro-2-methylpropanol (1 mole) gives sodium chloride (2 moles).

Experiment (iii). Radioactive 3-chloro-2-methylpropene (12 ml.) was added to a stirred solution (9 l.) of silver perchlorate (0·02M) and perchloric acid (0·02M) in a blackened vessel at 25°. 0·131M-Hypochlorous acid (8 × 50 ml.) was added during 3½ hr. Pure inactive 1 : 3-dichloro-2-methylpropan-2-ol (6·136 g.) was then added and the solution was extracted with pentane (500 g.). The pentane extract was dried and fractionated. There were recovered 1·7 g. of 3-chloro-2-methylpropene, b. p. 70—72°/760 mm., still slightly contaminated with pentane but completely free from other products. Samples of this, and of the original 3-chloro-2-methylpropene, were hydrolysed with sodium hydroxide in 50% ethanol. The solutions were just acidified with sulphuric acid, evaporated to dryness, and dissolved in water. The specific activities were found to be respectively 1933 ± 16 and 1911 ± 17, identical within statistical error.

The aqueous residue from the addition reaction, after extraction with pentane, was saturated with ether and then with sodium sulphate. The ether layer was removed and the aqueous solution was again extracted with ether (in all, 3½ l.). The ether solutions were combined, dried ($MgSO_4$), and fractionated. After removal of the ether, there was recovered 1 : 3-dichloro-2-methylpropan-2-ol, b. p. 60°/11 mm., n_D^{25} 1·4718, specific activity 879 ± 8. From the degree of dilution of the formed 1 : 3-dichloro-2-methylpropan-2-ol, the specific activity of which must be the same, on a molar basis, as that of the original 3-chloro-2-methylpropene, it can be calculated that from 0·0524 mole of hypochlorous acid there was produced 0·03655 mole (70%) of 1 : 3-dichloro-2-methylpropan-2-ol.

Subsidiary Experiment.—To show that exchange of ^{36}Cl between the two chlorohydrins during the working up of the reaction mixture is unimportant, the following experiment was performed. Labelled 1 : 3-dichloro-2-methylpropan-2-ol (specific activity, 21,470; 0·682 g.) was mixed with inactive 2 : 3-dichloro-2-methylpropanol (5·549 g.). The mixture (overall specific activity, 2374) was hydrolysed at 20° for 2 min. with enough alkali to decompose 10% of the dichlorohydrin. The residue was recovered and fractionated, early fractions being discarded and unchanged 2 : 3-isomer collected. After removal, by further alkaline hydrolysis, of the remaining contaminating 1 : 3-dichloro-2-methylpropan-2-ol, the residual material gave, on alkaline hydrolysis, chloride of specific activity 32. Thus the above procedure contaminates negligibly (*ca.* 1%, under the conditions of the above experiment) the 2-carbon atom of 2 : 3-dichloro-2-methylpropanol.

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Discussion

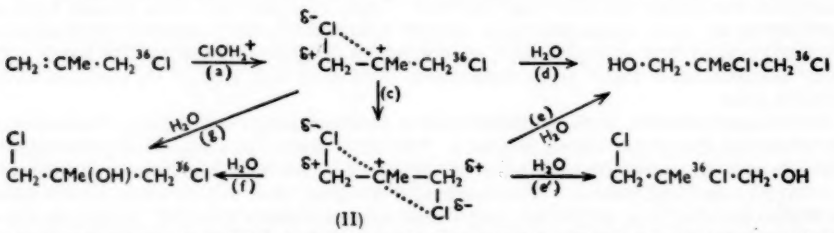
Formation of 2 : 3-*Dichloro-2-methylpropanol from Hypochlorous Acid and* 3-*Chloro-2-methylpropene.*—2 : 3-Dichloro-2-methylpropanol does not seem to have been characterised previously, though its dibromo-analogue has been prepared.[7] In the present work, it has been shown that it can be separated from its isomer, 1 : 3-dichloro-2-methylpropan-2-ol, by fractionation, and that it can be characterised and distinguished by its much slower rate of reaction with hydroxide ions in water. In these respects, it resembles its lower homologue.

Addition of hypochlorous acid, under catalysis by perchloric acid, to 3-chloro-2-methylpropene gives, as main product, 1 : 3-dichloro-2-methylpropan-2-ol. Under preparative conditions for addition of hypochlorous acid, this is well established from the work of other investigators. Kinetic analysis of the later chlorohydrin fractions from this reaction shows clearly, however, that 2 : 3-dichloro-2-methylpropanol is a minor product, amounting to about 6% of the total chlorohydrin produced. Addition to 3-chloropropene gives 70% of the analogous chlorohydrin,[3] so the presence of the 2-methyl substituent has modified the orientation considerably, in the direction that would be expected in view of the electron-donating capacity of this group.

Rearrangement accompanying Addition of Hypochlorous Acid to 3-*Chloro-2-methylpropene.*—In a previous paper,[3] it was argued that, in the absence of significant interaction between the entering electrophilic group, E, from the reagent EX, and the carbonium ionic centre, the orientation in addition to 3-chloropropene would be substantially the product of attachment of E to the 1-carbon atom. Still more should this be the case in the present example, and this can be supported by the experimental evidence that addition to this olefinic substance of hydrogen chloride gives 1 : 2-dichloro-2-methylpropane,[8] and addition of water gives 1-chloro-2-methylpropan-2-ol.[2]

The small amount of 2 : 3-dichloro-2-methylpropanol formed in the reactions described herein results, on the view proposed, from intermediates and by routes such as are indicated in the scheme below [sequences (a), (d), and (a), (c), (e) or (e′)].

Proposed sequence for reaction of hypochlorous acid with 3-*chloro-2-methylpropene.*



Two extreme results might be sought on this hypothesis. If reaction (d) occurred before the carbonium ion had time to acquire symmetry in reaction (c), then the 2-chlorine atom in the product would be derived entirely from the hypochlorous acid. If, on the other hand, the carbonium ion lasted long enough in solution to enable the 3-chlorine atom to become equivalent with the 1-chlorine atom, then any chlorine atoms ending up on the 2-position should, by way of such an intermediate as (II), have specific activity which was half that of the original 3-chloro-2-methylpropene.

In the present set of experiments, following the lines of the previous investigation, the specific activity has been examined of the 3-chlorine atom by converting the 2 : 3-dichloro-2-methylpropanol by alkaline hydrolysis into 1-chloro-2 : 3-epoxy-2-methylpropane,

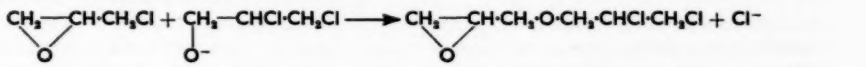
[6] Hearne and De Jong, *Ind. Eng. Chem.*, 1941, **33**, 940; Pritchard and Long, *J. Amer. Chem. Soc.*, 1956, **78**, 2667.
[7] Pogorshelski, *J. Russ. Phys. Chem. Soc.*, 1904, **36**, 1129.
[8] Burgin, Engs, Groll, and Hearne, *Ind. Eng. Chem.*, 1939, **31**, 1413.

and examining the specific activity of this material. The results, shown in the Tables, indicate that a sample of labelled 3-chloro-2-methylpropene of specific activity 4562 gave a combined dichlorohydrin fraction of specific activity 4538, unchanged within experimental error; and this, after dilution, gave 2 : 3-dichloro-2-methylpropanol of specific activity 160·3, from which was obtained 1-chloro-2 : 3-epoxy-2-methylpropane of specific activity 129·9. If the original addition of hypochlorous acid had proceeded entirely through a completely symmetrical intermediate (*e.g.*, II), then the specific activity of the recovered epoxide would have been 160·3/2 = 80·15. Hence the proportion of reaction proceeding through such an intermediate is (160·3—129·9)/(160·3—80·15) = 30·4/80·15 = 0·38; *i.e.*, 38%. The remainder must come by way of an unsymmetrical intermediate, *e.g.*, through reaction (d) of the scheme.

Previously [3] it was shown that the corresponding result for the reaction of 3-chloropropene with hypochlorous acid was 12%. The increased degree of rearrangement accompanying the addition to 3-chloro-2-methylpropene is in accordance with, and in the authors' view, supports the proposed mechanism. The 2-methyl substituent, being attached to the carbonium ionic centre in the intermediate, stabilises this and therefore this intermediate has a greater life in solution. As a consequence, the two chlorine substituents have more opportunity to become equivalent. It is noteworthy, however, that even in this tertiary carbonium ion, complete equivalence of the chlorine atoms is not achieved before reaction is completed by entry of the hydroxyl group.

It has been confirmed (experiment iii) that the first stage (a) of the addition reaction is not appreciably reversible, since, if it were, appreciable dilution of the 3-chloro-2-methylpropene would occur during the reaction by loss of the 3-chlorine atom, which can become, in part, structurally equivalent to the entering chlorine. In fact, excess of 3-chloro-2-methylpropene could be recovered unchanged in specific activity after the reaction. This experiment shows also that there is no adventitious dilution of the starting material during the reaction or in the working up.

Intermolecular Condensation during the Hydrolysis of 2 : 3-*Dichloro-2-methylpropanol.*—If the inorganic chloride derived from the 2 : 3-dichloro-2-methylpropanol under conditions of mild alkaline hydrolysis were representative of the chlorine from the 2-carbon atom, then the specific activity of this chloride would have been a direct measure of the extent of rearrangement. The value obtained by using the specific activity of sample 5 (see Table 2) is 45%, significantly higher than that derived from the measurement of the specific activity of the 1-chloro-2 : 3-epoxy-2-methylpropane. A similar, but greater discrepancy, was experienced in the earlier study [3,9] of the lower homologous system. In that case, the source of error was shown to be a side reaction, the cross-condensation, under conditions of mild alkaline hydrolysis, with bimolecular displacement at the terminal carbon atom, by such a reaction as the following :



In the present case, such side reactions are theoretically much less likely, for not only are the chlorohydrins themselves much more reactive in the competing internal nucleophilic displacements, but also the 2-methyl group must introduce steric hindrance [10] to displacement either at the 3- or at the 2-carbon atom. This theoretical justification is supported experimentally by the fact that the intramolecular condensation, to form 1-chloro-2 : 3-epoxy-2-methylpropane, of 1 : 2-dichloro-2-methylpropanol is accompanied by definite, but relatively small amounts of high-boiling material detectable by fractionation.

Elimination accompanying the Addition.—The dichlorohydrin mixture produced in the reaction accounts, as shown in experiment (iii), for 75% of the amount of hypochlorous acid used up in the reaction between this and excess of 3-chloro-2-methylpropene. The

[9] de la Mare and Pritchard, *J.*, 1954, 1644.
[10] Dostrovsky, Hughes, and Ingold, *J.*, 1948, 1283.

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remaining products of the reaction presumably result from elimination from the carbonium ion:

$$CH_2{=}CMe{\cdot}CH_2Cl \longrightarrow Cl{\cdot}CH_2{\cdot}^{+}CMe{\cdot}CH_2Cl \begin{cases} \nearrow\ CHCl{=}CMe{\cdot}CH_2Cl \\ \searrow\ CH_2{=}C(CH_2Cl)_2 \end{cases}$$

Other possibilities exist if hydrogen or chlorine migrates to the 2-position in the carbonium ion before elimination occurs. In Burgin, Hearne, and Rust's experiments,[2] such products might also have reacted, with chlorine, to give the tri- and tetra-chlorinated products which they isolated. Investigation of this aspect of the problem awaits further studies of the products of elimination from carbonium ions.[11]

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WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER ST., LONDON, W.C.1. [*Received, October 18th*, 1956.]

[11] Cf. de la Mare and Salama, *J.*, 1956, 3337.

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285. *Interaction between Phosphorus Halides and Alkoxytrimethylsilanes.*

By J. FERTIG, W. GERRARD, and H. HERBST.

Stepwise replacement of halogen in phosphorus trihalides has been effected by alkoxytrimethylsilanes, thus avoiding the presence of hydrogen halides or tertiary base. The 1-phenylethoxysilane afforded the dichloridite, but the *tert.*-butoxy-analogue gave only alkyl chloride. Replacement in the oxychloride proceeded to the dichloridate, and much more slowly to the chloridate, and there was evidence of formation of *n*-butyl phosphorodibromidate from the oxybromide. Fission of the alkoxysilane occurred differently in the examples of the 1-phenylethyl and diphenylmethyl derivatives, the oxychloride affording alkyl chloride and trimethylsilyl phosphorodichloridate.

REPLACEMENT of halogen in phosphorus trihalides and oxyhalides by the alkoxyl group has been effected by alkoxytrimethylsilane under conditions in which the presence of a tertiary base and a hydrogen halide is avoided. Certain limitations have been observed. Thus stepwise replacement of halogen in the trichloride by alkoxyl was effected by *n*-butoxytrimethylsilane, giving the alkyl phosphorodichloridite, the dialkyl phosphorochloridite, and the trialkyl phosphite [scheme (1)]. *n*-, *iso*-, and *sec.*-Butyl phosphorodibromidites, and the corresponding bromidites were prepared from phosphorus tribromide. The halogenotrimethylsilane formed concurrently was readily separated and used for the preparation of further supplies of the alkoxysilane.

(1) $$PCl_3 \xrightarrow{Me_3Si{\cdot}OR} PCl_2{\cdot}OR \xrightarrow{Me_3Si{\cdot}OR} PCl(OR)_2 \xrightarrow{Me_3Si{\cdot}OR} P(OR)_3$$

Even when the 1-carbon atom of the alkyl group is as reactive as that in 1-phenylethyl, the dichloridite is formed, although decomposition into alkyl chloride occurs slowly at 15° and more quickly on attempted distillation. However, *tert.*-butoxytrimethylsilane and phosphorus trichloride gave alkyl chloride without revealing even the transitory formation of a phosphorus ester; and diphenylmethoxytrimethylsilane behaved similarly.

Interaction of the alkoxysilanes with phosphorus oxychloride presented a novel feature depending on the relative reactivity of the 1-carbon atom in the alkyl group. With *n*-butoxytrimethylsilane, the first alkoxyl group was introduced smoothly [scheme (2)], but the second reaction (3) was very slow. The products from the 1-phenylethoxysilane

and diphenylmethoxysilane were alkyl chloride and trimethylsilyl phosphorodichloridate [reactions (4) and (5)], showing fission of the O–C rather than the O–Si bond. On the other

(2) $Bu^nO{\cdot}SiMe_3 + POCl_3 \longrightarrow ClSiMe_3 + POCl_2{\cdot}OBu^n$

(3) $Bu^nO{\cdot}SiMe_3 + POCl_2{\cdot}OR \longrightarrow ClSiMe_3 + POCl(OBu^n)_2$

hand *tert.*-butoxytrimethylsilane did not react with phosphorus oxychloride even at 110°. Models show that steric hindrance is the likely cause.

(4) $CHPhMe{\cdot}O{\cdot}SiMe_3 + POCl_3 \longrightarrow POCl_2{\cdot}O{\cdot}SiMe_3 + CHPhMeCl$

(5) $Ph_2CH{\cdot}O{\cdot}SiMe_3 + POCl_3 \longrightarrow POCl_2{\cdot}O{\cdot}SiMe_3 + CHPh_2Cl$

An attempt to convert the trimethylsilyl phosphorodichloridate into the diethyl ester, $Me_3Si{\cdot}O{\cdot}PO(OEt)_2$ by means of pyridine and ethanol was abortive, because the dichloridate reacted more quickly with the base itself (this being reminiscent of the interaction of *n*-butyl phosphorodichloridate and pyridine [1]) and led to formation of ethoxytrimethylsilane (reaction 6).

(6) $Me_3Si{\cdot}O{\cdot}POCl_2 + C_5H_5N \longrightarrow Me_3SiCl +$ (probably) $[O_2P{\cdot}NC_5H_5]^+Cl^-$

$Me_3SiCl + EtOH + C_5H_5N \longrightarrow Me_3Si{\cdot}OEt + C_5H_5N,HCl$

Phosphorus oxybromide (1 mol.) with *n*-butoxytrimethylsilane (1 mol.) at 0° afforded bromotrimethylsilane and *n*-butyl phosphorodibromidate (apparently the first example of an alkyl phosphorodibromidate). It decomposed steadily at 15° and quickly on attempted distillation, *n*-butyl bromide being a product. With butan-1-ol (2 mols.) and pyridine (2 mols.) it afforded tri-*n*-butyl phosphate. Gerrard and Jeacocke [2] were unable to isolate the dibromidate on interaction of phosphorus oxybromide and tri-*n*-butyl phosphate, although there was indication of its formation by the interaction of the oxybromide and alcohol. The oxybromide (1 mol.) and the silane (3 mols.) gave tri-*n*-butyl phosphate.

The preparation of alkyl phosphorodibromidites and bromidites in phosphorus tribromide–alcohol systems has been described by Gerrard and Herbst.[3]

Although tertiary base is avoided at the alkoxylation stage, it still must be used in the preparation of the alkoxytrimethylsilane, for owing to intervention by hydrogen chloride and the volatility of chlorotrimethylsilane, reaction (7) has not yet been made to proceed to the right to a satisfactory extent.[4]

(7) $Me_3SiCl + ROH \longrightarrow Me_3Si{\cdot}OR + HCl$

Experimental

Phosphorus Trichloride Systems.—*n*-Butoxytrimethylsilane (14·6 g., 1 mol.) was added dropwise to phosphorus trichloride (13·75 g., 1 mol.) at −10°, and after the mixture had remained at 15° for 12 hr. chlorotrimethylsilane (97·2%), b. p. 58—60° (Found: Cl, 32·5. Calc. for C_3H_9ClSi: Cl, 32·7%), and *n*-butyl phosphorodichloridite (88·6%), b. p. 68—70°/22 mm. (Found: Cl, 40·2; P, 17·6. Calc. for $C_4H_9OCl_2P$: Cl, 40·6; P, 17·7%), were obtained.

Similarly the silane (23·02 g., 2 mols. for 1 mol. of trichloride) afforded chlorotrimethylsilane (91·5%), b. p. 58—60° (Found: Cl, 32·3%) (withdrawn from the mixture at 20 mm. and trapped at −80°), *n*-butyl phosphorodichloridite (19·4%), b. p. 70—72°/22 mm. (Found: Cl, 40·4; P, 17·2%), di-*n*-butyl phosphorochloridite (27·3%), b. p. 96—104°/6 mm. (Found: Cl, 16·5; P, 14·4. Calc. for $C_8H_{18}O_2ClP$: Cl, 16·7; P, 14·6%), and tri-*n*-butyl phosphite (19·0%), b. p. 119—122°/12 mm. (Found: P, 12·6. Calc. for $C_{12}H_{27}O_3P$: P, 12·4%).

With the silane (14·6 g., 3 mols. for 1 mol. of trichloride) it was necessary to heat the mixture at 70° for 3 hr. to obtain a satisfactory replacement of the third chlorine atom. Separation of chloridite and phosphite was protracted. Besides the chlorotrimethylsilane, drawn off at

[1] Gerrard, *J.*, 1940, 1464.
[2] Gerrard and Jeacocke, *J.*, 1954, 3647.
[3] Gerrard and Herbst, *J.*, 1955, 277.
[4] Gerrard and Kilburn, *J.*, 1956, 1536.

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15 mm., tri-*n*-butyl phosphite (74·6%), b. p. 78°/0·2 mm., n_D^{20} 1·4324, d_4^{22} 0·9251 (Found: P, 12·8%), and a mixture of chloridite and phosphite (1·0 g.) were obtained.

After a mixture of tri-*n*-butyl phosphite (4·24 g., 1 mol.) and chlorotrimethylsilane (5·5 g., 3 mols.) had been heated at 90° (reflux) for 5 hr., the phosphite (3·9 g.), b. p. 76°/0·2 mm. (Found: P, 12·2%), and the chlorosilane (4·8 g.), b. p. 57° (Found: Cl, 32·1%), were recovered.

The butoxysilane (16·24 g., 1 mol.) was added to *n*-butyl phosphorodichloridite (19·46 g., 1 mol.) at −10°, and after the mixture had remained at 15° for 12 hr. chlorotrimethylsilane (96%), the dichloridite (3·7 g.) (Found: Cl, 40·2; P, 17·4%), the chloridite (7·45 g.) (Found: Cl, 16·8; P, 14·5%), and the phosphite (10·75 g.), b. p. 116—122°/9 mm. (Found: P, 12·6%), were isolated.

A mixture of the butoxysilane (14·6 g., 1 mol.) and the chloridite (21·3 g., 1 mol.) was heated at 65° for 5 hr. The chlorosilane (90·7%) and unchanged butoxysilane (1·1 g.), b. p. 115—120°, were removed at 20°/10 mm. (trap at −80°), and from the residue (24·85 g.) a mixture of chloridite and phosphite (2·5 g.), b. p. 103—118°/10 mm. (Found: Cl, 8·6%), and tributyl phosphite (20·55 g.), b. p. 120—122°/10 mm. (Found: P, 12·4%), were obtained.

By corresponding procedures *sec.*-butoxytrimethylsilane (14·6 g., 1 mol.) and phosphorus trichloride (13·75 g., 1 mol.) gave chlorosilane (97·2%), *sec.*-butyl phosphorodichloridite (79·4%), b. p. 61°/19 mm. (Found: Cl, 40·4; P, 17·5%), and a mixture (2·2 g.) of dichloridite and chloridite, b. p. 61—90°/19 mm. (Found: Cl, 29·0%).

When 3 mols. of silane (21·9 g.) were used for one of trichloride, chlorotrimethylsilane (66%) and unchanged silane (7 g.) were withdrawn at 20°/10 mm., and the residue afforded mixtures (total, 9·2 g.) of tributyl phosphite and chloridite, b. p. 98—112°/16 mm., which were very slowly separated into the constituents.

A mixture of *tert.*-butoxytrimethylsilane (7·30 g., 1 mol.) and trichloride (6·87 g., 1 mol.) was stored at 15° for 12 hr., and volatile matter was removed at 15°/15 mm. (trap at −80°). When a half of the material had evaporated, the remainder suddenly showed signs of decomposition, and there was a residue (1·5 g.) (Found: P, 36·6%). It was evident that the trap contents (12·61 g.) (Found: Cl, 40·4; P, 7·2%) comprised *tert.*-butyl chloride (4·2 g., 0·92 mol.), chlorosilane, and phosphorus trichloride, which would be extremely tedious to separate. By the addition of sufficient butan-1-ol and pyridine, pyridine hydrochloride (11·7 g., 1·96 mol.), containing the chlorine other than that in *tert.*-butyl chloride, was obtained, and from the filtrate tri-*n*-butyl phosphite (3·4 g.), b. p. 120°/10 mm. (Found: P, 13·0%), was isolated.

A mixture of trimethyl-1-phenylethoxysilane (9·7 g., 1 mol.) and trichloride (6·9 g., 1 mol.) was stored at 15° for 12 hr., and chlorotrimethylsilane (5·2 g., 96%), b. p. 57—61° (Found: Cl, 33·1%), was withdrawn at 25°/18 mm., leaving a residue (*A*) (vigorously shaken) which could not have contained phosphorus trichloride. To 4·0 g. of the residue, 1-phenylethanol (4·38 g.) and pyridine (2·38 g.) in ether were added at —10°, and base hydrochloride (3·9 g.) and a final residue (6·85 g., after being at 65°/0·2 mm. for 3 hr.) (Found: P, 8·0. Calc. for $C_{24}H_{27}O_3P$: P, 7·9%), n_D^{18} 1·5450 (identified as tri-1-phenylethyl phosphite), were separated (see Gerrard and Shepherd [5]). This result indicates that residue (*A*) was 1-phenylethyl phosphorodichloridite, but after it (10·2 g.) had been stored for several hours at 18°, phosphorus trichloride (2·2 g.), b. p. 76° (Found: Cl, 76·7; P, 21·8. Calc. for Cl_3P: Cl, 77·45; P, 22·55%), was withdrawn at 18°/15 mm.; from the residue, 1-chloro-1-phenylethane, b. p. 42°/0·1 mm. (Found: Cl, 25·0. Calc. for C_8H_9Cl: Cl, 25·3%), was distilled.

A mixture of diphenylmethoxytrimethylsilane (15·9 g., 1 mol.) and trichloride (8·60 g., 1 mol.) afforded chlorotrimethylsilane (88·4%; withdrawn at 18°/12 mm., final pressure being reduced to 0·05 mm.) and a residue (*B*) (16·35 g.) of which 5·85 g. gave chlorodiphenylmethane (1·23 g.), b. p. 104°/0·1 mm. (Found: Cl, 17·7. Calc. for $C_{13}H_{11}Cl$: Cl, 17·5%), and a final residue (2·58 g.) (Found: Cl, 6·6; P, 13·1%). Addition of diphenylmethanol (13·56 g.) and pyridine (5·82 g.) (in ether) to the residue (*B*) (10·5 g.) gave no base hydrochloride, thus showing absence of dichloridite and chloridite.

Phosphorus Oxychloride Systems.—The *n*-butoxysilane (21 g., 1 mol.) and oxychloride (11·6 g., 0·5 mol.) gave (12 hr. at 20°) chlorotrimethylsilane and unchanged silane (removed at 20°/15 mm. and trapped at −80°), *n*-butyl phosphorodichloridate (9·0 g.), b. p. 38—42°/0·08 mm. (Found: Cl, 36·5; P, 16·9. Calc. for $C_4H_9O_3Cl_2P$: Cl, 37·2; P, 16·2%), and di-*n*-butyl phosphorochloridate (4·1 g.), b. p. 70—72°/0·08 mm. (Found: Cl, 15·7; P, 14·05. Calc. for $C_8H_{18}O_3ClP$: Cl, 15·5; P, 13·6%). The chlorosilane (1 mol.) and the chloridate

[5] Gerrard and Shepherd, *J.*, 1953, 2069.

(1 mol.) were mixed, but were quantitatively separated after being at 20° or 60° for several hours.

The *iso*butoxysilane (14·6 g., 1 mol.) and phosphorus oxychloride (0·5 mol.) gave the dichloridate (5·1 g.), b. p. 36°/0·1 mm. (Found: Cl, 36·0%), and the chloridate (2·4 g.), b. p. 74°/0·1 mm. (Found: Cl, 17·0; P, 14·4%). A mixture of the dichloridate (8·1 g., 1 mol.) and the alkoxytrimethylsilane (1 mol.) was heated at 120° for 5 hr., whereafter the dichloridate (5·1 g.) was recovered and the chloridate (3·5 g.), b. p. 74°/0·1 mm., was obtained. The *sec.*-butoxysilane (7·3 g., 1 mol.) and phosphorus oxychloride (7·7 g., 1 mol.) afforded the dichloridate (8·6 g., 90%), b. p. 46°/4 mm. (Found: Cl, 37·0; P, 16·4%), after the mixture had been heated at 75° for 6 hr. Chlorotrimethylsilane (94·5%), b. p. 58—62° (Found: Cl, 32·5%), was withdrawn at 20°/12 mm.

Diphenylmethoxytrimethylsilane (12·8 g., 1 mol.) and the oxychloride (7·7 g., 1 mol.) were mixed and heated at 100° for 4 hr., whereafter *trimethylsilyl phosphorodichloridate* (6·1 g., 59·4%), b. p. 40°/0·1 mm. (Found: Cl, 34·3; P, 14·8. $C_3H_9O_2Cl_2PSi$ requires Cl, 34·3; P, 14·9%), and chlorodiphenylmethane (8·66 g., 85·3%), b. p. 96°/0·02 mm. (Found: Cl, 17·5%), were obtained.

The silyl phosphorodichloridate decomposes slowly at 15°, and to some extent on distillation. In the attempt to prepare the diethyl trimethylsilyl phosphate, the dichloridate (8·05 g., 1 mol.) was added to ethanol (3·6 g., 2 mols.) and pyridine (6·1 g., 2 mols.) in ether (30 c.c.) at −10°. The white solid (9·8 g.), which was formed immediately, contained phosphorus (Found: Cl, 25·2: P, 9·3: C_5H_5N, 59·6%); the residue (3·9 g.) from evaporation of the filtrate gave only ethoxytrimethylsilane (3·5 g.), b. p. 73—76°, and an undistillable residue containing phosphorus.

It was then shown that the dichloridate (3·45 g., 1 mol.) reacted immediately with pyridine (1·32 g., 1 mol.) at −15° and afforded chlorotrimethylsilane (1·4 g. 78·2%), b. p. 57—60° (Found: Cl, 32·3), and a solid (2·91 g.) (Found: Cl, 18·4; P, 18·9; C_5H_5N, 48·1%) containing all the phosphorus and pyridine and half of the chlorine in the system. A solid of similar composition was formed when pyridine (2 mol.) was added to the dichloridate (1 mol.).

Trimethyl-1-phenylethoxysilane also afforded the trimethylsilyl phosphorodichloridate and alkyl chloride.

Phosphorus Tribromide Systems.—The silane and tribromide (1 mol.) were mixed slowly at 15°, and after 6 hr. the bromotrimethylsilane (90—97%), b. p. 79—80° (Found: Br, 52·3 ± 0·3. Calc. for C_3H_9BrSi: Br, 52·3%), was withdrawn at 15°/5 mm. and condensed at −79°. Results are recorded in the Table. The bromidite was accompanied by dibromidite.

R in $Me_3Si\cdot OR$	Mols.	Yield (%)	B. p. (mm.)	n_D^{20}	Found: Br (%)	Calc.: Br (%)
Dibromidites $PBr_2\cdot OR$						
Bu^n	1	79	38° (0·01)	1·5445	60·3	60·6
Bu^s	1	77	38 (0·1)	1·5410	60·7	—
Bu^i	1	81	37 (0·01)	1·5389	63·3	—
$C_6H_{13}\cdot CHMe$	1	51	76 (0·05)	1·5115	49·2	50·0
Bromidites $PBr(OR)_2$						
Bu^n	2	68	54 (0·06)	1·4689	30·9	31·1
Bu^s	2	66	44 (0·1)	1·4590	31·6	—
Bu^i	2	69	41 (0·04)	1·4536	31·4	—

n-*Butoxytrimethylsilane and Phosphorus Oxybromide.*—The silane (6·6 g., 1 mol.) was added to the oxybromide [6] (13·0 g., 1 mol.) at −10°. Bromotrimethylsilane (5·9 g., 85·5%) was withdrawn at 15°/15 mm. and condensed at −80°, giving a residue (12·7 g.) of n-*butyl phosphorodibromidate* (Found: Br, 53·4; P, 10·9. $C_4H_9O_2Br_2P$ requires Br, 57·2; P, 11·1%), which afforded *n*-butyl bromide on attempted distillation; this gave tri-*n*-butyl phosphate (5·7 g., 71·3%), b. p. 98°/0·1 mm. (Found: P, 11·4. Calc. for $C_{12}H_{27}O_4P$: P, 11·65%), and pyridine hydrobromide (9·0 g., 96·8%) when it (8·34 g., 1 mol.) in ether (50 c.c.) was added to butan-1-ol (4·3 g., 2 mols.) and pyridine (4·7 g., 2 mols.) in ether (25 c.c.) at −10°. After the dibromidate (3·6 g.) had been stored at 15° for 7 days, *n*-butyl bromide (1·5 g., 80%), b. p. 101° (Found: Br, 58·1. Calc. for C_4H_9Br: Br, 58·3%), was withdrawn at 15°/0·2 mm., leaving a solid (1·8 g.) (Found: Br, easily hydrolysed, 30·8; P, 18·5%).

The oxybromide (8·3 g., 1 mol.) in ether (20 c.c.) was added to the silane (12·7 g., 3 mols.)

[6] Gerrard, Nechvatal, and Wyvill, *Chem. and Ind.*, 1947, 437.

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in ether (20 c.c.). After 16 hr. at 15°, bromotrimethylsilane (9·1 g., 69%), b. p. 76—78° (Found: Br, 51·5. Calc. for C_3H_9BrSi: Br, 52·4%), and tri-*n*-butyl phosphate (5·4 g., 70%), b. p. 90°/0·01 mm. (Found: P, 11·5%), were obtained. The low yield of the purified bromosilane is due to the difficulty in separating it from the solvent.

Preparation of the Silanes.—These were prepared by the addition of chlorotrimethylsilane (1 mol.) to a solution of the alcohol (1 mol.) and pyridine (1 mol.) in pentane. A number of alkoxytrimethylsilanes containing phenyl-substituted alkyl groups were thus made by Gerrard and Kilburn;[4] others are: *n*-butoxytrimethylsilane, b. p. 124°, n_D^{20} 1·3927, sec.-*butoxytrimethylsilane*, b. p. 112·3°, n_D^{20} 1·3898, d_D^{22} 0·772 (Found: C, 58·0; H, 12·35. $C_7H_{18}OSi$ requires C, 57·5. H, 12·3%), *iso*butoxytrimethylsilane, b. p. 112·7°, n_D^{20} 1·3880, d_D^{22} 0·770 (Found: C, 58·2; H, 12·6%), *trimethyl-2-methylheptyloxysilane*, b. p. 91°/22 mm., n_D^{20} 1·4124, d_4^{20} 0·7937 (Found: C, 65·4; H, 12·5; Si, 13·65. $C_{11}H_{26}OSi$ requires C, 65·3; H, 12·9; Si, 13·85%).

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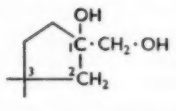
286. *Cafestol. Part II.** †

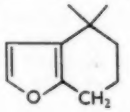
By R. D. HAWORTH and R. A. W. JOHNSTONE.

The conversion of cafestol into the tetrabasic acid (XII; R = R′ = H) has been effected by two alternative three-stage oxidation processes. Selenium dehydrogenation of this acid yielded, with other unidentified products, 4 : 5-benzindan-1-one (XV) and 1-ethyl-2-methylnaphthalene. Unless migration of alkyl groups is assumed the formation of the last compound cannot be explained on the basis of structure (V), recently suggested by Djerassi and his colleagues,[1] but the dehydrogenation may be readily interpreted on the basis of structure (IX) which is now advanced.

As a result of earlier work * it was concluded that cafestol had the molecular formula $C_{20}H_{28}O_3$ and probably contained the partial structures (I) and (II), although it was realised that quaternary carbon atoms postulated in each fragment depended on inconclusive evidence arising from the oxidative fission of the rings to acids containing hindered, and probably tertiary, carboxyl groups. Dehydrogenations of cafestol or of an anhydro-lactone derivative failed to throw light on the main skeleton although a diterpenoid structure was suspected. Djerassi and his co-workers [1] have recently subjected to selenium dehydrogenation a derivative of cafestol prepared by oxidising the partial structure (I) to the dibasic acid of partial structure (III). The isolation of 2-hydroxyphenanthrene and 1-ethyl-2-hydroxyphenanthrene from the dehydrogenation



(I)



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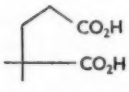


(III)

established both the pentacyclic nature of cafestol and the position of the furan ring, and led to the partial structure (IV). The five-membered ring glycol was considered to be attached to a bridgehead position as in structure (V) in order to account for several observations including (*a*) the infrared spectroscopic determination of one *C*-methyl group in epoxynorcafestadiene (VI) and (*b*) the formation of a tribromo-substitution product from epoxynorcafestanone (VII). The position of the angular methyl group was selected on the basis of an assumed biogenetic analogy with the phyllocladene system (VIII), but the location of the angular methyl group in phyllocladene has not been established.

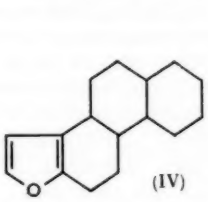
* Part I, *J.*, 1955, 1983.

† A preliminary account was published in *Chem. and Ind.*, 1956, 168.

[1] Djerassi, Bendis, and Sengupta, *J. Org. Chem.*, 1955, **20**, 1046; Bendis and Djerassi, *Chem. and Ind.*, 1955, 1483.

These investigations partly forestalled and overlapped our work which has confirmed the conclusions of Djerassi and his co-workers as far as the attachment of the furan ring and the five-membered ring glycol are concerned. But structure (V) does not contain the fragment (II) the presence of which was rendered probable by our earlier experiments, and for some time we had favoured the modified phyllocladene structure (IX) which is strongly supported by recent dehydrogenation experiments.

Epoxynorcafestadienone (X), prepared by the action of lead tetra-acetate on cafestol,[2] was converted by ozone into the dicarboxylic acid (XI), which was oxidised by potassium hypoiodite to the tetrabasic acid (XII; R = R′ = H). This acid (XII; R = R′ = H) was amorphous and probably composed of a mixture of epimeric forms. On methylation with diazomethane it gave a tetramethyl ester (XII; R = R′ = Me), which was hydrolysed by sodium hydroxide to the amorphous dimethyl ester (XII; R = Me, R′ = H), two ester groups resisting hydrolysis in accordance with the proposed structures. Similar products were obtained by an alternative route involving hypoiodite oxidation of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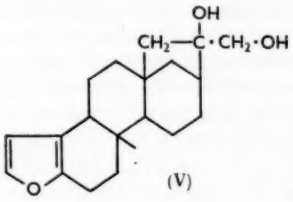
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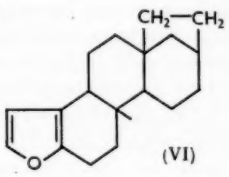
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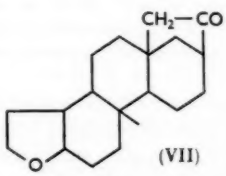
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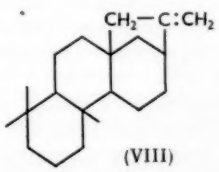
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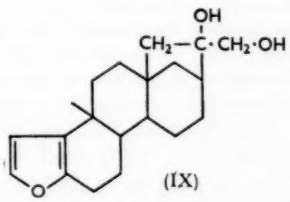
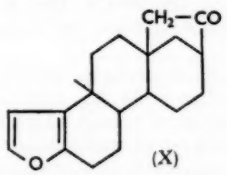

(IX)

epoxynorcafestadienone (X) to the dicarboxylic acid (XIII),[1] the dimethyl ester [1] of which was ozonised to the dibasic acid (XIV) yielding the tetramethyl ester (XII; R = R′ = Me) and dimethyl ester (XII; R = Me, R′ = H) on methylation and subsequent hydrolysis, respectively.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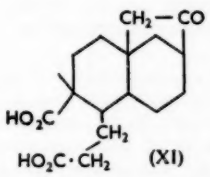
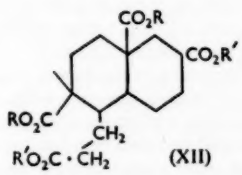

(XI)

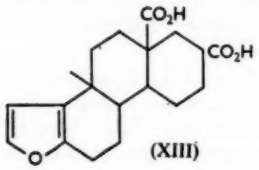

(XII)

The tetrabasic acid (XII; R = R′ = H) was dehydrogenated with selenium and the products separated by the combined use of the Girard-T reagent, vacuum distillation, chromatographic adsorption on alumina, and vapour-phase chromatography (cf. Experimental section).

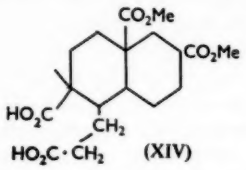
The ketonic fraction yielded 4 : 5-benzindan-1-one (XV) identified by comparison of the ketone and its 2 : 4-dinitrophenylhydrazone with synthetic specimens.[4] A small quantity of an unidentified six-membered ring ketone, $C_{15}H_{22}O_2$, was also isolated from the ketonic fraction. The benzindanone (XV) is obviously derived from the tetrabasic

[2] Wettstein, Fritzsche, Hunzicker, and Miescher, *Helv. Chim. Acta*, 1941, **24**, 332F.

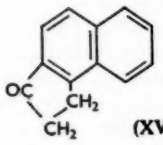
acid (XII; R = R′ = H) by cyclisation to the five-membered ring ketone, decarboxylation, and dehydrogenation, and its formation is not only consistent with structure (IX) and (XII; R = R′ = H) for cafestol and the tetrabasic acid, respectively, but proves



(XIII)



(XIV)



(XV)

that the methyl group in cafestol must be attached to an angular position from which it is eliminated during the dehydrogenation.

The main dehydrogenation product, however, was a hydrocarbon which showed three main regions of ultraviolet absorption at 220, 280, and 320 mμ characteristic of naphthalenes, and the ε value (794) of the 320 mμ band suggested a di- or tri-alkylated structure.[5] The hydrocarbon was identified as 1-ethyl-2-methylnaphthalene by comparison of the picrate and trinitrobenzene adduct with synthetic specimens. A viscous oil giving a crystalline but unidentified trinitrobenzene complex was also isolated, and small amounts of either 1- or 2-methylnaphthalene, and traces of two other non-identified products were detected by vapour-phase chromatography in the hydrocarbon fractions. The production of 1-ethyl-2-methylnaphthalene can be readily understood on the basis of formula (XII; R = R′ = H) for the tetrabasic acid, and, in the absence of migration phenomena, it establishes the position of the angular methyl group in cafestol (IX). In order to derive the hydrocarbon from other cafestol structures such as (V) it would be necessary to assume that the 2-methyl group was produced by reduction of a carboxyl group as has occasionally been observed[6] during selenium dehydrogenation experiments. This alternative explanation is, however, disposed of by the absence of polymethylnaphthalenes from the dehydrogenation products.

This structure (IX), like that suggested for methyl vinhaticoate, is not divisible into *iso*prene units. It is possible that these structures are derived from diterpenoid frameworks by migration of groups during the formation of the aromatic furan ring. Alternatively the structures may be derived by the combination of a pentose fragment with three *iso*pentane units.

Experimental

Cafestol, prepared from Green Santos Bourbon coffee beans as described in Part I, was oxidised by lead tetra-acetate to epoxynorcafestadienone,[2] which was ozonised and converted into the dibasic acid (XI).[3]

Oxidation of the Dibasic Acid (XI).—The dibasic acid (XI) (1·7 g.) in methanol (50 ml.) was treated simultaneously with a solution of iodine (5·5 g.) in methanol (50 ml.) and one of potassium hydroxide (4·5 g.) in methanol (50 ml.) containing water (3 ml.), both added dropwise and at room temperature during 1½ hr. with continuous stirring which was continued for 1½ hr. after completion of the addition. The mixture was poured into water (1 l.) containing a slight excess of sulphuric acid, the solution extracted several times with chloroform, and the combined extracts washed with successive small quantities of sodium thiosulphate solution and water. The chloroform solution was then extracted with dilute sodium hydroxide, from which the tetrabasic acid (XII; R = R′ = H) was recovered by acidification and isolated with chloroform. The colourless or light tan-coloured amorphous acid (1 g.) when methylated with

[3] Wettstein, Hunzicker, and Miescher, *Helv. Chem. Acta.*, 1943, **26**, 1197.
[4] Cook and Hewitt, *J.*, 1934, 365; Fieser and Gates, *J. Amer. Chem. Soc.*, 1940, **62**, 2335.
[5] Morton and de Gouveia, *J.*, 1934, 916; see also Friedel and Orchin, "Ultra-violet Spectra of Aromatic Compounds," John Wiley & Sons, New York.
[6] Windaus and Thiele, *Annalen*, 1936, **521**, 160; Wiesner, Armstrong, Bartlett, and Edwards, *J. Amer. Chem. Soc.*, 1954, **76**, 6068.

diazomethane in ether gave the *tetramethyl ester* (XII; R = R′ = Me) as a viscous liquid, b. p. 165° (bath temp.)/5 × 10^{-5} mm. (Found: C, 61·1; H, 7·8; MeO, 28·1. $C_{21}H_{32}O_8$ requires C, 61·1; H, 7·8; 4MeO, 30·0%).

Hydrolysis of the Tetramethyl Ester (XII; R = R′ = Me).—The tetramethyl ester (140 mg.) in methanol (6 ml.) was refluxed with N-sodium hydroxide (3 ml.) for 3 hr., and, after dilution with water (150 ml.), neutral material was removed in ether. The aqueous solution was acidified and extracted with ether–chloroform (1 : 2 v/v), and the extract dried (Na_2SO_4). Removal of the solvent and crystallisation from light petroleum (b. p. 40—60°) gave the dibasic *acid* (XII; R = Me, R′ = H) as micro-crystals, m. p. 58—63° (Found: equiv., 198. $C_{19}H_{28}O_8$ requires equiv., 192).

Oxidation of the Dimethyl Ester of Acid (XIII).—The dimethyl ester [1] (340 mg.) in ethyl acetate (50 ml.) was treated with sufficient ozone for the saturation of three double bonds at the temperature of acetone–solid carbon dioxide. The solvent was removed under reduced pressure at room temperature, and the ozonide heated on a steam-bath for 1 hr. with water (10 ml.) containing hydrogen peroxide (0·5 ml. of 100 vol.). The cooled solution was extracted with chloroform, the extract was washed with N-sodium hydroxide, and the washings acidified with dilute hydrochloric acid. The solution was extracted with chloroform, the extract dried (Na_2SO_4), and the solvent removed, leaving the dimethyl ester (XIV) as a colourless amorphous residue (290 mg.). This ester when esterified with ethereal diazomethane gave the tetramethyl ester (XII; R = R′ = Me), b. p. 160—170° (bath temp.)/5 × 10^{-5} mm., which was hydrolysed to the dibasic acid (XII; R = Me, R′ = H), m. p. 58—66° (Found: equiv., 194).

Reduction of the Dimethyl Ester of Acid (XIII).—The dimethyl ester (600 mg.) in methanol (10 ml.) and ethyl acetate (10 ml.) was hydrogenated at room temperature and pressure in the presence of 10% palladium–charcoal catalyst (700 mg.); the *tetrahydro-derivative* obtained by reduction of the furan ring was a viscous liquid, b. p. 180° (bath temp.)/0·7 mm. (Found: C, 69·0; H, 8·9. $C_{21}H_{32}O_5$ requires C, 69·2; H, 8·9%).

Action of Selenium on the Tetrabasic Acid (XII; R = R′ = H).—A typical experiment only is described. The tetrabasic acid (XII; R = R′ = H) (5·5 g.) was heated with selenium (9 g.) for 24 hr. at 330—340°. The mixture was extracted with ether, and the extract was washed successively with dilute sodium hydroxide solution and water and dried (Na_2SO_4). The ether was removed, the oily residue taken up in light petroleum (b. p. 40—60°), and the solution shaken with mercury (5 ml.) for 20 hr. to remove hydrogen selenide. The solvent was removed and the residue separated into ketonic and hydrocarbon fractions by treatment with Girard-T reagent.

The Girard-T extract was decomposed by contact with 0·5N-hydrochloric acid for 1 hr., and the ketonic products isolated with ether, dried, and sublimed at 160° (bath temp.)/10 mm. The sublimate yielded, after further sublimation and crystallisation from methanol, 4 : 5-benzindan-1-one as needles (15 mg.), m. p. 119—120°, alone or admixed with an authentic specimen,[6] and the ultraviolet spectrum showed maxima at 228 mμ (ε 28,180), 248 mμ (ε 30,900), and 280 mμ (ε 10,000). The 2 : 4-*dinitrophenylhydrazone* separated from benzene–ethanol in red needles, m. p. and mixed m. p. 300° (Found: N, 15·5. $C_{19}H_{14}O_4N_4$ requires N, 15·5%). The residue from the sublimation was recrystallised several times from ether and gave a small quantity of colourless needles, m. p. 196—197° (Found: C, 77·0; H, 9·6. $C_{18}H_{22}O_2$ requires C, 76·9; H, 9·4%), which showed in the infrared spectrum a single band at 1720 $cm.^{-1}$ indicative of six-membered ring carbonyl absorption. This *ketone*, m. p. 196—197°, which gave a yellow 2 : 4-dinitrophenylhydrazone, was not identical with that, m. p. 196—198°, prepared as described by Djerassi, Wilfred, Visco, and Lemin.[7]

The hydrocarbon fraction was an oil, which was taken up in light petroleum (b. p. 40—60°), adsorbed on a small column of alumina and separated by elution with ether into two fractions: (a) a colourless liquid with a faint blue fluorescence and a naphthalene odour and (b) a viscous yellow fluorescent liquid with an odour reminiscent of pinacol.

Fraction (a) was distilled at 85—100°/0·05 mm., and the small residue (X) added to fraction (b); the colourless distillate (250 mg.) was converted into the trinitrobenzene adduct which separated from methanol in yellow needles, m. p. 117° undepressed by admixture with the trinitrobenzene complex prepared from synthetic 1-ethyl-2-methylnaphthalene.[8] The

[7] Djerassi, Wilfred, Visco, and Lemin, *J. Org. Chem.*, 1953, **18**, 1449.

[8] Brunner and Grof, *Monatsh.*, 1934, **64**, 76; Kloetzel, *J. Amer. Chem. Soc.*, 1940, **62**, 1711; Adkins and Davies, *ibid.*, 1949, **71**, 2955.

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adduct, which in the ultraviolet region showed bands at 228 mμ (ε 100,000), 280 mμ (ε 10,720), and 321 mμ (ε 6761), was decomposed by passing an ethereal solution through alumina, and gave 1-ethyl-2-methylnaphthalene as an oil showing peaks in the ultraviolet spectrum at 226 mμ (ε 70,790), 280 mμ (ε 6310), 319 mμ (ε 794), and which gave a picrate, m. p. and mixed m. p. 111°. The remainder of fraction (a) was investigated by vapour-phase chromatography.

Fraction (b) [and the small residue (X) from fraction (a)] was separated by fractional distillation into fraction (b i) (20 mg.), b. p. 100—120° (bath temp.)/0·05 mm., giving a very small amount of a trinitrobenzene adduct, m. p. 123°, and investigated further by vapour-phase chromatography, and fraction (b ii), a green-yellow fluorescent viscous oil (50 mg.), b. p. 160—180° (bath temp.)/0·05 mm., which gave a trinitrobenzene adduct, separating from methanol in orange needles, m. p. 130° (Found, on a small quantity: C, 56·9; H, 4·8%), which showed strong maxima in the ultraviolet region at 233, 255, 272, 285, 300, 319, 326, 329, and 335 mμ.

Vapour-phase Chromatography.—The column (100 cm. × 0·7 cm.) was packed with silicone high-vacuum grease on Celite 535 (0·4 : 1 w/w), and after model experiments with carefully purified synthetic naphthalenes the following conditions were adopted. The samples (less than 0·05 ml.) were introduced by means of a hypodermic needle, the column temperature was 212°, a carrier gas (nitrogen) flow rate of approx. 25 ml./min. and a pressure drop in the column of 170 mm. were used; the retention times (min.) were: mesitylene 7, 1-methyl- 21·5, 2-methyl- 22, 1-ethyl- 38, and 1-ethyl-2-methyl-naphthalene 41.

Fraction (a), mixed with a little mesitylene, gave the following peaks with a flow rate of 25 ml./min.

TABLE 1.

Peak	Retention time (min.)	Assignment	Quantity
1	7	Mesitylene	Standard
2	21·5	1- or 2-Methylnaphthalene	Small quantity
3	30	?	Trace
4	41	1-Ethyl-2-methylnaphthalene	Major product
5	50·5	?	Trace

Peaks 3 and 5 were present in extremely small quantities and were not identified; peak 3, however, is not 1- or 2-ethylnaphthalene.

Fraction (b i), mixed with a little mesitylene, gave the following peaks with a flow rate of 22 ml./min.

TABLE 2.

Peak	Retention time (min.)	Assignment	Quantity
1	7·5	Mesitylene	Standard
2	42·5	1-Ethyl-2-Methylnaphthalene	Trace
3	56·5	identical with fraction 5 of Table 1	Small quantity but more than in Table 1

Our thanks are due to the University of Sheffield for the award of a Henry Ellison Fellowship (to R. A. W. J.), to Imperial Chemical Industries Limited for a grant, to Dr. J. W. Cook, F.R.S., for a gift of β-1-naphthylpropionic acid from which a specimen of 4 : 5-benzindan-1-one was synthesised, and to Dr. J. M. Tedder for his interest in the vapour-phase chromatographic work.

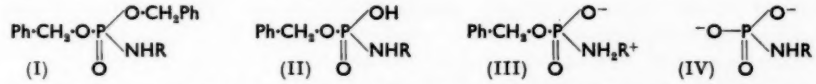
THE UNIVERSITY, SHEFFIELD, 10. [*Received, November 7th*, 1956.]

287. *Studies on Phosphorylation. Part XV.* The Use of Phosphoramidic Esters in Acylation. A New Preparation of Adenosine-5′ Pyrophosphate and Adenosine-5′ Triphosphate.*

By V. M. Clark, G. W. Kirby, and Sir Alexander Todd.

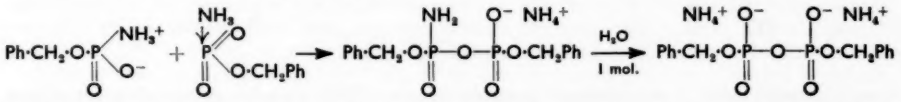
The monobenzyl esters of phosphoramidic and certain *N*-substituted phosphoramidic acids behave as selective acylating agents for phosphoric acid anions; alcoholic hydroxyl groups present are unaffected. By their use nucleoside polyphosphates can be readily synthesised from unprotected nucleotides. In particular adenosine-5′ phosphate (AMP) can be converted into adenosine-5′ pyrophosphate (ADP) and thence into adenosine-5′ triphosphate (ATP) in high yield.

While investigating the selective anionic debenzylation of the dibenzyl esters of phosphorus-containing acids it was shown [1] that the esters of certain phosphoramidic acids, *e.g.*, (I; R = H), gave rise to a series of mono-de-esterified products (II) which behaved, apparently, as zwitterions (III). It was suggested that such systems might behave as acylating agents, being closely related to the base–metaphosphate complexes investigated in preliminary fashion by Langheld,[2] who showed that ethyl metaphosphate (presumably in polymeric form) gave complexes with amines and amino-acids although



these complexes were not characterised. That the system (II/III) might have zwitterionic character is supported by the *X*-ray crystallographic work of Hobbs, Corbridge, and Raistrick [3] on the monosodium salt of phosphoramidic acid itself in which it was shown that the $^{+}NH_3 \cdot PO_3^{-}$ ion has a 3-fold symmetry, the arrangement of bonds around both the N and P atoms being tetrahedral.

Our initial experiments were directed towards the phosphorylation of alcohols by the monobenzyl ester of phosphoramidic acid (II/III; R = H); when its solution in benzyl alcohol was heated no detectable acylation of the solvent occurred but the crystalline diammonium salt of P^1P^2-dibenzyl pyrophosphate separated. In dioxan at 100°, separation of this salt began within a few minutes and in two hours it was formed in high yield. Re-examination of the original specimen of monobenzyl phosphoramidate, isolated as the hemihydrate some five years earlier [1] and stored in a stoppered tube without any special precautions, showed that this, too, with the passage of time had been largely converted into diammonium P^1P^2-dibenzyl pyrophosphate. The formation of this product is presumably attributable to interaction of the anionic oxygen atom of one molecule with the electrophilic phosphorus atom of the other, followed by hydrolysis of the remaining $>PO \cdot NH_2$ grouping and formation of the ammonium salt, as shown.



Detailed consideration of the mechanism of formation must await a kinetic analysis of this reaction but the occurrence of phosphorylation of an anionic species by the monoester of a phosphoramidic acid is not in doubt.

* Part XIV, *J.*, 1956, 3524.

[1] Clark and Todd, *J.*, 1950, 2031.
[2] Langheld, *Ber.*, 1910, **43**, 1857; 1911, **44**, 2076.
[3] Hobbs, Corbridge, and Raistrick, *Acta Cryst.*, 1953, **6**, 621.

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These preliminary observations suggested that the monoesters of the phosphoramidic acids would react with phosphate anions to yield pyrophosphates and that alcoholic groups also present would be unaffected. This selectivity would make them particularly suited to the synthesis of nucleoside polyphosphates and unsymmetrical pyrophosphates of the nucleotide coenzyme type.

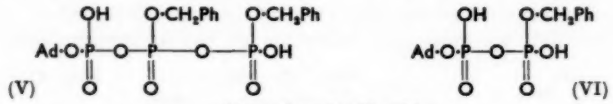
The early work of Stokes [4] indicated that preliminary addition of a proton is of importance in this acylation and our observations suggest that the site of the proton is also relevant to the course of reaction. Stokes showed that the dianion of phosphoramidic acid is extremely stable in aqueous solution, the acid yielding but 3% of its nitrogen as ammonia after treatment with hot concentrated potassium hydroxide for one hour; in contrast, the monoprotonated anion, $\{[NH_2 \cdot P(O)O_2^{--}][H^+]\}$ undergoes hydrolysis to orthophosphate merely on recrystallisation of its potassium salt. In ten minutes at 100°, 98% of the nitrogen is available as ammonia.

A proton, added to the anion of a phosphoramidic acid (IV), can become attached to an oxygen atom (cf. II) or to the nitrogen atom (cf. III), according to their relative basicities, but only in the latter case would the product be a phosphorylating agent. Substitution of the nitrogen atom by an aryl residue would be expected to decrease the possibility of adding a proton to nitrogen and in accordance with this we find that benzyl hydrogen *N*-phenylphosphoramidate gives very much lower yields of pyrophosphate in the presence of phosphate anions.

With the pyridinium salt of adenosine-5′ phosphate dissolved in dimethylformamide, a variety of *N*-substituted monobenzyl phosphoramidates gave the monobenzyl ester of adenosine-5′ pyrophosphate as the major product, although some di(nucleoside-5′) pyrophosphate was also formed, presumably through anhydride–anion exchange: [5] the amount of this by-product could be considerably diminished by adding small amounts of water. Uridine-5′ phosphate was phosphorylated in analogous fashion, yielding P^1-benzyl P^2-uridine-5′ pyrophosphate and di(uridine-5′) pyrophosphate. In none of these reactions could acylation of alcoholic groups be detected. The monoesters of *N*-benzyl-, *N-cyclo*hexyl-, and the unsubstituted phosphoramidic acid gave comparable results as phosphorylating agents, but the *N*-phenyl derivative was much less effective.

By using benzyl hydrogen phosphoramidate and the pyridinium salt of adenosine-5′ phosphate in dimethylformamide containing 5% of water it was possible, after removal of the benzyl group by catalytic hydrogenation, to isolate lithium adenosine-5′ pyrophosphate in 48% yield. Analogously, by using benzyl hydrogen *N-cyclo*hexylphosphoramidate and the tri-*n*-butylammonium salt of adenosine-5′ pyrophosphate in dry dimethylformamide, adenosine-5′ triphosphate has been obtained in 71% yield (isolated as its lithium salt). In the last reaction some higher adenosine polyphosphates are also produced.

From these observations it appears that monobenzyl phosphoramidates phosphorylate nucleotides in step-wise fashion: thus, adenosine-5′ phosphate (AMP) was converted into



Ad = adenosine-5′ residue

a monobenzyl ester of adenosine-5′ pyrophosphate (ADP) without appreciable formation of esters of adenosine-5′ triphosphate (ATP), and similarly, ADP yielded a benzyl ester of ATP as the major product although in both experiments an excess of phosphoramidate was present. The observations suggest that, under the particular experimental conditions, the dibenzyl ester (V) of ATP is unstable relative to the monoester (VI) of ADP.

[4] Stokes, *Amer. Chem. J.*, 1893, **15**, 198; cf. Muller, Rathly, and Rosenberg, *Biochim. Biophys. Acta*, 1956, **19**, 563.
[5] Corby, Kenner, and Todd, *J.*, 1952, 1234.

These investigations demonstrate the utility of monoesterified phosphoramidates in the phosphorylation of unprotected nucleoside phosphates and indicate that nucleoside phosphoramidates might be used in the synthesis of unsymmetrical pyrophosphates.

In a note published some time after completion of this work, Chambers and Khorana [6] recorded their preliminary observations that certain monosalts of phosphoramidic acid react with orthophosphoric acid to yield pyrophosphates and with AMP to yield a mixture of ADP, ATP, higher polyphosphates, and unchanged AMP in approximately equal amounts. They have also indicated the formation of ADP from the interaction of adenosine-5′ phosphoramidate and orthophosphoric acid. Baddiley, Buchanan, and Letters [7] have shown that *N*-phosphoryl derivatives of glyoxaline can be used in phosphorylation though, in this case, the systems are to be compared with mixed anhydrides, and, characteristically being less selective, acylate alcoholic groups as well as acid anions. The *di*esters of *N*-phosphorylglyoxaline are themselves phosphorylating agents whereas the *di*esters of phosphoramidic acid appear not to be.

Experimental

Benzyl Hydrogen Phosphoramidate.—Its hemihydrate [1] was obtained (Found: equiv., 196. Calc. for $C_7H_{10}O_3NP,\frac{1}{2}H_2O$: equiv., 196). After drying for 4 days (P_2O_5/0·1 mm.) the *anhydrous compound* was obtained (Found: C, 44·8; H, 5·4; N, 7·3%; equiv., 182. $C_7H_{10}O_3NP$ requires C, 44·9; H, 5·4; N, 7·5%; equiv., 187).

Benzyl Hydrogen N-Benzylphosphoramidate.—Dibenzyl *N*-benzylphosphoramidate [8] was monodebenzylated by lithium chloride according to Clark and Todd's method.[1] To the ice-cold solution of the crude lithium salt (2·5 g.) in water (40 c.c.) excess of hydrochloric acid (3N) was added whereupon *benzyl hydrogen N-benzylphosphoramidate* (1·7 g.) was precipitated; it was washed with water and dried *in vacuo* (P_2O_5). Recrystallisation from ethyl acetate gave prisms, m. p. 98—100° (varying with the rate of heating) (Found: C, 59·0; H, 5·7; N, 4·9. $C_{14}H_{16}O_3NP,\frac{1}{2}H_2O$ requires C, 58·8; H, 5·9; N, 4·9%).

Benzyl Hydrogen N-cycloHexylphosphoramidate.—Dibenzyl *N-cyclo*hexylphosphoramidate [8] was debenzylated by lithium chloride, and the free acid isolated (75% yield) as described above for the *N*-benzyl derivative. Recrystallised from ethyl acetate *benzyl hydrogen N-cyclohexylphosphoramidate* was obtained as needles, m. p. 101—104° (Found: C, 58·0; H, 7·6; N, 5·5. $C_{13}H_{20}O_3NP$ requires C, 58·0; H, 7·4; N, 5·2%).

Benzyl Hydrogen N-Phenylphosphoramidate.—The lithium salt [1] of this acid was converted into the silver salt by treatment with aqueous silver nitrate, and a suspension of this salt in chloroform was then decomposed by passage of hydrogen sulphide. After 1 hr. the precipitate was filtered off and extracted with ethanol. Evaporation of the ethanol gave benzyl hydrogen *N*-phenylphosphoramidate as pale yellow crystals whose *cyclo*hexylamine salt, crystallised from ethanol–acetone, had m. p. 178—179°, undepressed on admixture with that obtained by Clark and Todd.[1]

Diammonium P^1P^2*-Dibenzyl Pyrophosphate.*—Tetrabenzyl pyrophosphate [9] (0·20 g.) was heated under reflux for 2 hr. in ethyl methyl ketone (2 c.c.) containing ammonium thiocyanate (57 mg.), and the *diammonium* P^1P^2*-dibenzyl pyrophosphate* which separated was filtered off, washed with ethyl methyl ketone until colourless, and dried *in vacuo* at room temperature (0·11 g., 78%). Recrystallised from aqueous acetone it formed plates, m. p. 220° (decomp.) (Found: C, 42·6; H, 6·0; N, 6·6. $C_{14}H_{22}O_7N_2P_2$ requires C, 42·9; H, 5·6; N, 7·1%).

Effect of Heat on Benzyl Hydrogen Phosphoramidate in Dioxan Solution.—Benzyl hydrogen phosphoramidate (0·10 g.) was heated at 100° in dioxan solution for 2 hr. The colourless crystals which separated were washed with dioxan, then with ether, and dried (0·07 g.). Recrystallised from aqueous acetone they formed plates, m. p. 216° (decomp.), whose aqueous solution was neutral, and whose infrared spectrum was identical with that of diammonium

[6] Chambers and Khorana, *Chem. and Ind.*, 1956, 1022.
[7] Baddiley, Buchanan, and Letters, *J.*, 1956, 2812.
[8] Atherton, Openshaw, and Todd, *J.*, 1945, 660.
[9] Kenner, Todd, and Weymouth, *J.*, 1952, 3675.

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P^1P^2-dibenzyl pyrophosphate (Found: C, 42·6; H, 5·6; N, 7·0. Calc. for $C_{14}H_{22}O_7N_2P_2$: C, 42·9; H, 5·6; N, 7·1%).

Adenosine-5′ Pyrophosphate.—Adenosine-5′ phosphate (300 mg. of monohydrate) was converted into its dipyridinium salt by dissolution in water (2—3 c.c.), addition of excess (3 drops) of pyridine, evaporation at room temperature, and drying over phosphoric oxide. The salt, a brittle glass, was suspended in dimethylformamide (40 c.c.) containing water (2 c.c.), and benzyl hydrogen phosphoramidate (600 mg.; 3·5 mols.) was added. The suspension was slowly heated to 70° to effect solution and was then kept at 95—100° for 5 hr. Solvent was removed under reduced pressure at 40° and the residue dissolved in water, the pH being adjusted to 4—5 by initial addition of pyridine followed by acetic acid. Hydrogenation at room temperature and atmospheric pressure with 10% palladised charcoal (10 mg.) together with palladous oxide (60 mg.) brought about complete removal of benzyl groups; after 5 hr. the solution was filtered and adjusted to pH 5, and one-half of it subjected to ion-exchange chromatography on a Dowex-2 column (7·5 × 1·8 cm., Cl^- form). Elution with 0·003M-hydrochloric acid gave unchanged adenosine-5′ phosphate (42 mg.) and some orthophosphate: with 0·01M-hydrochloric acid containing 0·01M-lithium chloride a small quantity (5 mg.) of di(adenosine-5′) pyrophosphate was obtained followed by adenosine-5′ pyrophosphate (85 mg.). The elution was followed, and the yields were estimated, by measuring light absorption at 260 mμ. Each eluate was neutralised with lithium hydroxide and evaporated to small volume under reduced pressure at 50°, and the lithium salts were precipitated by addition of acetone–ethanol (3 : 1). Centrifugation of the adenosine-5′ pyrophosphate fraction followed by washing with acetone and drying (P_2O_5) gave the lithium salt of ADP in 48% yield (based on AMP). A portion of this lithium salt was converted into the free nucleotide by means of a Dowex-50 column in the acid form, the eluate being freeze-dried. Examination by paper electrophoresis at pH 4·8 and chromatography on Whatman No. 1 paper with butan-1-ol–acetic acid–water (5 : 2 : 3) showed the product to be indistinguishable from ADP and to contain no other ultraviolet-absorbing or phosphorus-containing component (Found: C, 26·6; H, 3·7; N, 15·2; P, 14·0. Calc. for $C_{10}H_{15}O_{10}N_5P_2,H_2O$: C, 27·0; H, 3·8; N, 15·7; P, 13·9%). Electrophoresis in 0·1M-potassium cyanide showed the synthetic material to travel appreciably slower than a mixture of adenosine-2′ : 5′ and adenosine-3′ : 5′ diphosphate.

Adenosine-5′ Triphosphate.—A solution of adenosine-5′ pyrophosphate (150 mg.) was obtained by decomposing an aqueous suspension of its barium salt with an equivalent amount of sulphuric acid (N/50); after removal of barium sulphate by centrifugation, the aqueous solution was treated with a slight excess of tri-*n*-butylamine in ether, and the resulting aqueous layer evaporated under reduced pressure at 40°, the residue being dried over phosphoric oxide. The glassy salt so obtained was dissolved in dry dimethylformamide (35 c.c.) containing benzyl hydrogen *N-cyclo*hexylphosphoramidate (490 mg., *ca.* 5 mols.), and the solution heated at 70° for 2 hr. After removal of solvent at 40°/1 mm. the resulting gum was suspended in water and brought into solution by dropwise addition of dilute aqueous ammonia; adjustment to pH 4 (by glacial acetic acid) was followed by hydrogenation at room temperature and atmospheric pressure with a palladous oxide catalyst (46 mg.). Hydrogen uptake was complete in 13 hr. The catalyst was filtered off, the pH adjusted to pH 9 by aqueous ammonia, and the solution subjected to ion-exchange chromatography on a column (7·5 × 1·8 cm.) of Dowex-2 resin (Cl^- form). Elution with 0·003M-hydrochloric acid gave adenosine-5′ phosphate (5 mg.) together with orthophosphate; with 0·01M-hydrochloric acid containing 0·01M-lithium chloride di(adenosine-5′) pyrophosphate (3 mg.) and unchanged adenosine-5′ pyrophosphate (13 mg.) were obtained; with 0·01M-hydrochloric acid containing 0·10M-lithium chloride adenosine-5′ triphosphate (127 mg.) was obtained. Elution with M-hydrochloric acid gave higher adenosine polyphosphates (20 mg.).

The ATP was isolated as its lithium salt (71%; cf. ADP), evaporation of the neutralised eluate being carried out at 40°. Adding barium acetate solution at pH 6 to an aqueous solution of the lithium salt precipitated the barium salt of ATP. After centrifugation it was washed first with 50% ethanol, then with 95% ethanol, and dried (over P_2O_5) (Found: N, 8·0; total P, 10·6; easily hydrolysed P,[10] 6·7%; *M*, 895, 878.[11] Calc. for $C_{10}H_{12}O_{13}N_5P_3Ba_2,6H_2O$: N, 7·9; total P, 10·5; easily hydrolysed P, 7·0%; *M*, 885). The lithium salt appeared chromatographically homogeneous in three different solvent systems (see below) and was

[10] Allen, *Biochem. J.*, 1940, **34**, 858.
[11] From absorbance at 260 mμ.

unresolved by electrophoresis at pH 4·8. After conversion of the synthetic material into its sodium salt by ion-exchange and treatment with 8-hydroxyquinoline to remove traces of heavy-metal impurities, inorganic phosphate was liberated from it by L-myosin [12] at a rate 82% of that observed for chromatographically pure ATP of natural origin.

Paper-chromatographic and Electrophoretic Data.—Electrophoretic buffer systems. A, acetate buffer at pH 4·8; B, 0·1M-potassium cyanide solution. Electrophoretic runs were carried out on Whatman No. 54 paper at 5 v/cm. for 7 hr.

Solvent systems for paper chromatography. C, butan-1-ol–acetic acid–water (5 : 2 : 3); D, propan-2-ol–1% aqueous ammonium sulphate (3 : 2) run on paper previously soaked in 1% ammonium sulphate solution and dried; E, *iso*butyric acid–N-ammonia–0·1M-ethylenediaminetetra-acetic acid [13] (100 : 60 : 1·6). Ascending chromatograms were run on Whatman No. 1 paper throughout, phosphorus being detected by the molybdate spray.[14]

Results are tabulated.

	Migration (cm.) in buffer		R_F in solvent		
	A	B	C	D	E
Adenosine-5′ phosphate	3·1	—	0·24	0·45	0·53
Adenosine-5′ pyrophosphate	6·8	8·8	0·12	0·33	0·39
Adenosine-5′ triphosphate	8·6	—	0·06	0·20	0·30
Di(adenosine-5′) pyrophosphate	4·1	—	—	—	—
Adenosine-(2′ or 3′)5′ diphosphate	—	11·8	—	—	—

Reaction of Benzyl Hydrogen Phosphoramidate with Adenosine-5′ Phosphate and Uridine-5′ Phosphate.—The nucleoside-5′ phosphate (10 mg.) as its pyridinium salt was heated in dimethylformamide solution (2—3 c.c.) with a variety of benzyl hydrogen phosphoramidates (3 mols.) for 3 hr. at 90—100°. The products were examined by paper chromatography in the butan-1-ol–acetic acid–water (5 : 2 : 3) system, the nucleotides being observed under filtered ultraviolet light (mercury lamp). Qualitative assessment gave the annexed results :

	Unchanged nucleoside-5′ phosphate	Monobenzyl ester of nucleoside-5′ pyrophosphate	Di-(nucleoside-5′) pyrophosphate
UMP in dry dimethylformamide	++	++++	+
AMP in dry dimethylformamide	++	+++	++
AMP in dimethylformamide containing 5% of water	+++	++++	Trace
AMP in dimethylformamide containing 15% of water	+++++	++	None detectable

Benzyl hydrogen phosphoramidate and the corresponding *N*-benzyl and *N-cyclo*hexyl derivatives gave comparable results, whereas the *N*-phenyl analogue gave much less pyrophosphate. Varying amounts of pyridine were added to a mixture of adenosine-5′ phosphate and benzyl hydrogen phosphoramidate (up to an excess of 7 mols.) without significantly affecting the result.

Grateful acknowledgment is made to the Department of Scientific and Industrial Research for a Maintenance Allowance and to Gonville and Caius College for the award of the Dunlop Studentship (to G. W. K.). Our thanks are also offered to Dr. S. V. Perry for enzymic tests.

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[12] Perry, "Methods in Enzymology," Academic Press, New York, 1955, Vol. II, p. 582.
[13] Krebs and Hems, *Biochim. Biophys. Acta*, 1953, **12**, 172.
[14] Hanes and Isherwood, *Nature*, 1949, **164**, 1107.

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288. *The Structure of the Major Component Glyceride of Cocoa Butter, and of the Major Oleodisaturated Glyceride of Lard.*

By D. Chapman, A. Crossley, and A. C. Davies.

It was recently suggested that the major glyceride of cocoa butter, long known to be one of the three possible oleopalmitostearins, is the 2-palmitate. From cooling curves and *X*-ray and infrared analyses, it is now concluded that the glyceride is the 2-oleate. Similar observations on the disaturated glycerides of lard show, in agreement with other workers, that the major disaturated glyceride is 2-palmito-oleostearin.

Cocoa butter is known to contain a high proportion of a single glyceride. Probably as a consequence of this, it exhibits marked polymorphism, and melts over a comparatively narrow temperature range. It is brittle at room temperature and completely molten at body temperature. For this and other reasons, it has found considerable application in confectionery products, particularly chocolate, and has been often investigated.

It was earlier concluded that more than 50% of the total glycerides of cocoa butter consists of one oleopalmitostearin, generally as a result of examination of hydrogenated fractions of cocoa butter. Amberger and Bauch [1] (also see Lewkowitsch [2]) found 57% of an oleopalmitostearin in cocoa butter. Amberger and Bauch [1] isolated a hydrogenated fraction of m. p. 63·5° and Lewkowitsch [2] concluded that this indicated the presence of 1-palmitodistearin (m. p. 65°) derived from 2-stearo-oleopalmitin or 2-oleopalmitostearin in the original cocoa butter. Hilditch and Stainsby's analysis [3] indicated oleopalmitostearin 52%, oleodistearin 19%, dioleostearin 12%, palmito-oleopalmitins 9%, oleodipalmitins 6%, and palmitostearins 2%. A more recent analysis by Meara [4] showed oleopalmitostearin 57%, oleodistearin 22%, oleodipalmitin 4%, dioleopalmitin 7%, dioleostearin 6%, triolein 1%, and saturated glycerides 3%. Both Hilditch and Stainsby [3] and also Meara [4] isolated, from hydrogenated fractions, material of m. p. 66—67° which they considered to consist largely of 2-palmitodistearin (m. p. 68°) derived from 2-palmito-oleostearin in the cocoa butter.

Lard is more variable in composition than cocoa butter. However, its glycerides are characterised by considerable contents of an oleopalmitostearin and dioleopalmitin. Thus a typical lard [5] contained oleopalmitostearin 34%, dioleopalmitin 40%, dioleostearin 5%, oleodipalmitin 9%, triolein 3%, and saturated glycerides 9%. Meara,[6] on the basis of the m. p., and Quimby, Wille, and Lutton [7] on the basis of *X*-ray data and cooling curves of hydrogenated lard fractions, were of the opinion that lard consists mainly of 2-palmito-glycerides.

In the present work the structure of the major glyceride of cocoa butter, and the major glyceride present in the disaturated glycerides of lard, have been re-investigated by cooling curves and *X*-ray and infrared analysis.

Experimental

The sample of cocoa butter used (I val., 36·0; sap. val., 194·4; free fatty acid, 0·7% as oleic) had the following component acids: saturated 62·4; oleic 33·2; linoleic 4·4. A second sample of cocoa butter (I val., 36·4; sap. val., 192·9; free fatty acid, 0·1% as oleic), used in several of the experiments, gave very similar results and led to the same conclusions.

Oleodisaturated Glycerides of Cocoa Butter.—A concentrate of the disaturated glycerides was

[1] Amberger and Bauch, *Z. Untersuch. Nahr. Genuz.*, 1924, **48**, 371.
[2] Lewkowitsch, *J. Soc. Chem. Ind.*, 1933, **52**, 236T.
[3] Hilditch and Stainsby, *J. Soc. Chem. Ind.*, 1936, **35**, 95T.
[4] Meara, *J.*, 1949, 2154.
[5] Hilditch and Pedelty, *Biochem. J.*, 1940, **34**, 971.
[6] Meara, *J.*, 1945, 23.
[7] Quimby, Wille, and Lutton, *J. Amer. Oil Chemists' Soc.*, 1953, 186.

prepared by crystallisation from acetone. Cocoa butter (150 g.) was crystallised from acetone (10 ml./g.) at 0°; the solid fraction was recrystallised similarly; the two liquid fractions (I val., 50·1) comprised 26·9% of the original cocoa butter. The solid fraction from the second crystallisation was then recrystallised from acetone (10 ml./g.) at 15°, to yield fractions comprising 7·7% and 65·4% of the cocoa butter, and having I val. 28·3 and 31·5 respectively. The latter fraction contained a high proportion of the disaturated glycerides of the cocoa butter.

Oleodisaturated Glycerides of Lard.—A concentrate of the disaturated glycerides of lard (I val., 67·0; free fatty acid, 0·2% as oleic) was made by crystallising 895 g. from acetone (10 ml./g.) at 0°. The solid fraction (239 g.) was recrystallised from acetone (6 ml./g.) at 22·5° and the resulting solid (77 g.; I val., 24·5) was again recrystallised from acetone (6 ml./g.) at 23°. The last two liquid fractions (180 g.) were recrystallised from acetone (5 ml./g.) at 0°, to yield a fraction of I val. 35·0 (19% of the original lard), containing a high concentration of disaturated glycerides.

Preparation of 2-Oleodistearin, 2-Oleodipalmitin, 2-Oleopalmitostearin, 2-Palmito-oleostearin, and 2-Stearo-oleopalmitin.—For the synthesis of these glycerides, highly purified samples (see Table; theor. or recorded values in parentheses) of oleic, palmitic, and stearic acids were prepared by conventional means.

	Setting pt.	Acid value	Sap. value	I value	Linoleic [9] acid (%)
Palmitic ...	62·25° (62·6) [8]	218·3 (219·2)	218·4 (219·2)	0·1 (0·0)	—
Stearic	69·25 (69·4) [8]	197·8 (197·5)	197·3 (197·5)	0·0 (0·0)	—
Oleic	—	—	—	89·6 (89·9)	0·5 (0·0)

The palmitoyl and stearoyl chlorides required were prepared by treating the acids with thionyl chloride. They were rapidly distilled under a high vacuum, from a pre-heated bath. The distilled products contained *ca.* 1% of free fatty acid, as determined by Bauer's anilide method.[10] Oleoyl chloride, prepared [11] by treating oleic acid with thionyl chloride in benzene, was distilled as above and contained 1—2% of free acid.

(a) *2-Oleodistearin and 2-oleodipalmitin.* 1-Monostearin and 1-monopalmitin, prepared by Baer and Fischer's method,[12] contained 100% of monoglyceride as determined by the periodate method [13] and had m. p. 81·5° (cf. 81·5° [14]) and 77° (cf. 77° [14]), respectively.

1 : 3-Distearin and 1 : 3-dipalmitin were prepared by a similar method to that of Malkin.[15] The monoglycerides were treated with an equimolar amount of the acid chloride in pyridine–chloroform at 10—15° for 2 hr. The diglycerides were crystallised successively from alcohol and hexane at room temperature, to constant m. p. and hydroxyl value [1 : 3-distearin, m. p. 80·0° (cf. ref. 16), OH val. 89, I val. 0; 1 : 3-dipalmitin, m. p. 74·0° (cf. ref. 16), OH val. 96, I val. 0·0].

The diglycerides were refluxed with an excess of oleoyl chloride in pyridine–chloroform,[16] passed in light petroleum (b. p. 40—60°) (4 ml./g.) through alumina (twice wt. of glyceride; activated at 800°), eluted with light petroleum, and crystallised from acetone (15 ml./g.) at 0°. This removed traces of diglyceride and avoided the necessity for repeated crystallisation. 2-Oleodistearin and 2-oleodipalmitin had respectively m. p. 42·5°, 36·5° (cf. ref. 16), I val. 28·5, 30·2, and sap. val. 189·8, 202·8.

(b) *2-Oleopalmitostearin, 2-palmito-oleostearin, and 2-stearo-oleopalmitin.* 1-Palmito-3-stearin was prepared from 1-monopalmitin and stearoyl chloride as described above. 1-Oleo-3-stearin and 1-oleo-3-palmitin were prepared from 1-monostearin and 1-monopalmitin respectively by 1 mol. of oleoyl chloride in the same manner, except that the reaction temperature was allowed to rise to 30° (no appreciable formation of triglyceride); the products, crystallised at 0° from alcohol and then from hexane, had the properties tabulated (cf. refs. 17 and 18).

[8] Francis and Piper, *J.*, 1939, 577.
[9] Hilditch, Patel, and Riley, *Analyst*, 1951, **76**, 81.
[10] Bauer, *Oil and Soap*, 1946, **23**, 1.
[11] Human and Mills, *Nature*, 1946, **158**, 877.
[12] Baer and Fischer, *J. Amer. Chem. Soc.*, 1945, **67**, 2031.
[13] Pohle, Mehlenbacher, and Cook, *Oil and Soap*, 1945, **22**, 115.
[14] Malkin and Shurbagy, *J.*, 1936, 1628.
[15] Malkin, *J.*, 1937, 1412.
[16] Craig, Lundberg, and Geddes, *J. Amer. Oil Chemists' Soc.*, 1952, **29**, 169.
[17] Verkade and van der Lee, *Rec. Trav. chim.*, 1936, **55**, 267.
[18] Daubert and Longenecker, *J. Amer. Chem. Soc.*, 1944, **66**, 53.

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	M. p.	OH val.	I val.
1-Palmito-3-stearin	71·5°	93·5	0·0
1-Oleo-3-stearin	49	90	40·6
1-Oleo-3-palmitin	44	96	42·4

They were converted into triglycerides by treatment with the requisite acid chloride.[18] The products were purified as before by alumina and crystallisation from acetone, their properties being (cf. ref. 19):

	M. p.	I val.	Sap. val.
2-Oleopalmitostearin	37·5—38°	29·2	194·7
2-Palmito-oleostearin	40·5—41	29·4	195·1
2-Stearo-oleopalmitin	41—41·5	29·3	195·3

X-Ray diffraction data on the triglycerides are also tabulated. The spacings were in close agreement with the data recorded by Lutton.[20]

Synthetic Mixtures.—Synthetic mixtures (see Table) were made, of pure oleodisaturated glycerides, having compositions resembling approximately those of cocoa butter and of its constituent disaturated glycerides, based on Meara's [4] analysis of cocoa butter.

Mixture:	A	B	C	D	E
2-Oleopalmitostearin	55	—	—	69	—
2-Oleodistearin	21	21	21	26	26
2-Oleodipalmitin	4	4	4	5	5
2-Palmito-oleostearin	—	55	—	—	69
2-Stearo-oleopalmitin	—	—	55	—	—
Fr. of I val. 50·1 from cocoa butter	20	20	20	—	—

Cooling Curves.—The fat (15 g.), melted at 100°, was weighed into a 4½ × 1″ test-tube and allowed to cooled to 41°; the tube was fixed in an air-bath maintained at 19°; the fat was then stirred by a gentle stroke of a ring stirrer every 15 sec., readings of the temperature being taken every minute. Stirring was continued until the sample was too stiff, generally before the maximum temperature (after supercooling) was reached.

X-*Ray Diffraction Spectra.*—A Metro-Vick *X*-ray unit with Cu-*K*α radiation was used, the sample-to-film distance being 12·5 cm. Only the more stable forms of the pure glycerides and fats were examined. Samples were normally prepared by slow crystallisation from a solvent, but it was more convenient in certain cases to use samples which had been stored in the solid state for a considerable time.

X-*Ray diffraction data.*

Cocoa butter	Fract.[1]	Mixture A	Mixture B	Mixture C	Mixture D	Mixture E	POS[a] (β-3)	OPS[b] Sub. β′3	OPS[b] β′3	OSP[c] β′-2	Lard fract.[2]
Short spacings (Å)											
5·45 s	5·36 m	5·41 s	—	5·30 mw	5·39 m	5·25 w	5·40 m	—	—	5·45 w	5·36 vw
5·20 w	5·11 w	5·11 m	—	5·08 vw	5·11 m	—	5·11 w	5·08 w	—	5·10 w	4·99 w
4·68 } vs	4·59 vs	4·63 } vs	4·70 s	4·85 vw	4·65 } vs	4·70 s	4·57 s	4·73 s	4·65 m	4·43 ms	4·66 ms
4·54 }	—	4·53 }	4·57 s	4·60 s	4·52 }	4·47 } m	4·38 m	4·47 s	4·52 w	4·32 ms	
4·28 w	4·27 w	4·24 vw	4·42 s	4·40 s	4·35 vw	4·32 }	4·22 m	4·27 } vs	4·41 w	4·15 ms	4·13 vs
—	—	4·08 w	—	4·22 s	4·23 w	—	—		4·17 vs	4·03 ms	
4·02 s	3·96 mw	3·97 s	4·20 s	3·92 s	3·98 m	4·15 } vs	4·02 ms	4·08 }	4·05 m	3·84 s	
3·90 ms	3·85 mw	3·85 m	4·07 s	3·87 s	3·85 mw	4·05 }	3·89 w	3·84 s	4·00 m	3·67 w	—
3·79 ms	3·74 m	3·74 m	4·01 m	3·75 ms	3·72 mw	3·88 ms	3·84 w	3·74 s	3·80 ms	—	3·80 ms
3·68 s	3·66 m	3·65 s	3·88 w	3·60 w	3·65 s	3·77 ms	3·67 m	—	3·69 ms	—	3·72 ms
			3·80 s								
			3·70 s								
Long spacings (Å)											
64·5	64·5	64·1	68·9	43·7	64·1	68·9	64·1	69·4	66·9	43·7	69·4

[1] Cocoa butter fraction of I value 31·5. [2] Lard fraction of I val. 35·7.
[a] 2-Oleopalmitostearin. [b] 2-Palmito-oleostearin. [c] 2-Stearo-oleopalmitin.

Infrared Spectra.—A Grubb-Parsons S.3 infrared spectrometer was used with a rock-salt prism, for the range 1800—650 cm.$^{-1}$, with capillary thicknesses of sample between rock-salt

[18] Verkade, *Rec. Trav. chim.*, 1943, **62**, 393.
[20] Lutton, *J. Amer. Chem. Soc.*, 1951, **73**, 5595.

flats. The sample could be prepared as for the *X*-ray diffraction measurements, but for investigating polymorphic changes the rock-salt flats were enclosed in a cell the temperature of which could be varied.

Results and discussion

Cocoa butter, the crystallised cocoa butter fraction, and the crystallised lard fraction have been examined. Comparisons were made with pure samples of the three isomeric

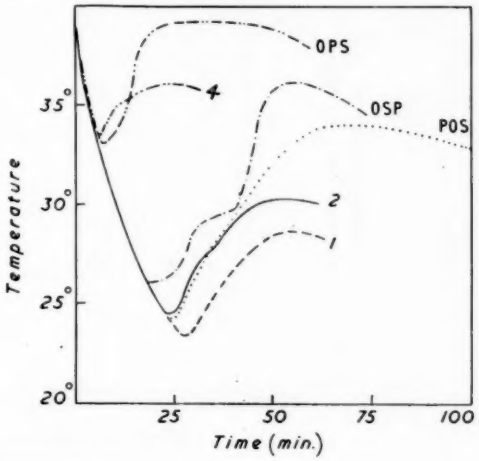

FIG. 1. *Cooling curves of pure glycerides, cocoa butter, and lard fraction.*

1, *Cocoa butter.*
2, *Cocoa butter fraction.*
3, *Synthetic mixture* A.
4, *Lard fraction.*
POS, 2-*oleopalmitostearin.*
OSP, 2-*stearo-oleopalmitin.*
OPS, 2-*palmito-oleostearin.*

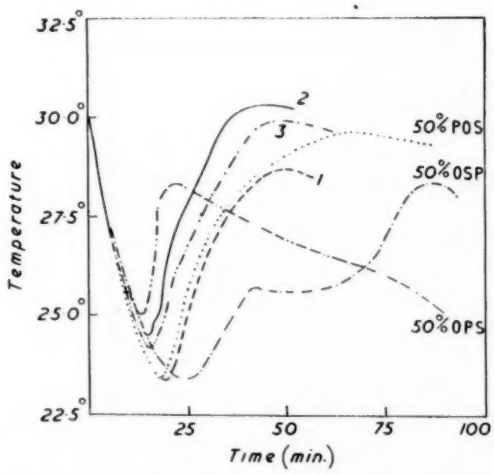

FIG. 2. *Cooling curves of mixtures of pure glycerides with cocoa butter.*

For key, see Fig. 1.

oleopalmitostearins and with synthetic mixtures of pure glycerides mixed in approximately the same proportions in which they occur in cocoa butter.

Cooling Curves.—The cooling curve of a fat or fat fraction is frequently of assistance in determining the nature of the glycerides present (cf. Quimby *et al.*[7]). The curves for cocoa butter and the cocoa butter fraction of I value 31·5 have been compared with those for the three oleopalmitostearins (Fig. 1) and 1 : 1 mixtures of each of these glycerides with cocoa butter (Fig. 2).

The curve for 2-oleopalmitostearin closely resembles that for cocoa butter and the cocoa butter fraction, whereas the curves for 2-stearo-oleopalmitin and particularly for

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FIG. 3.

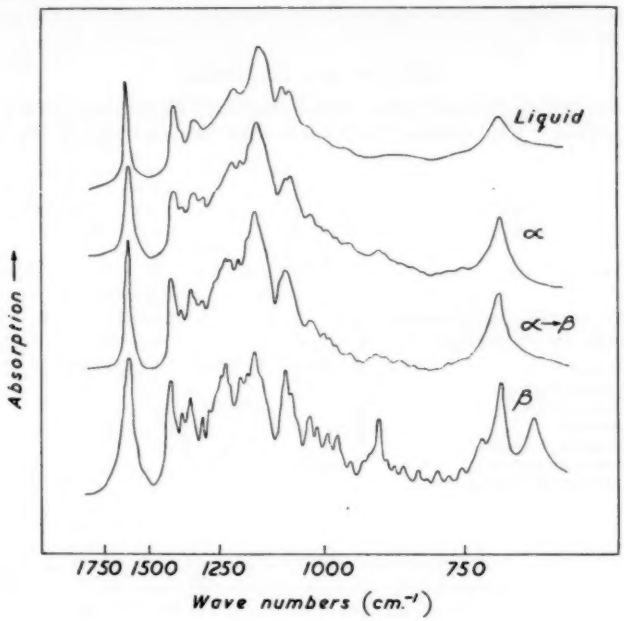
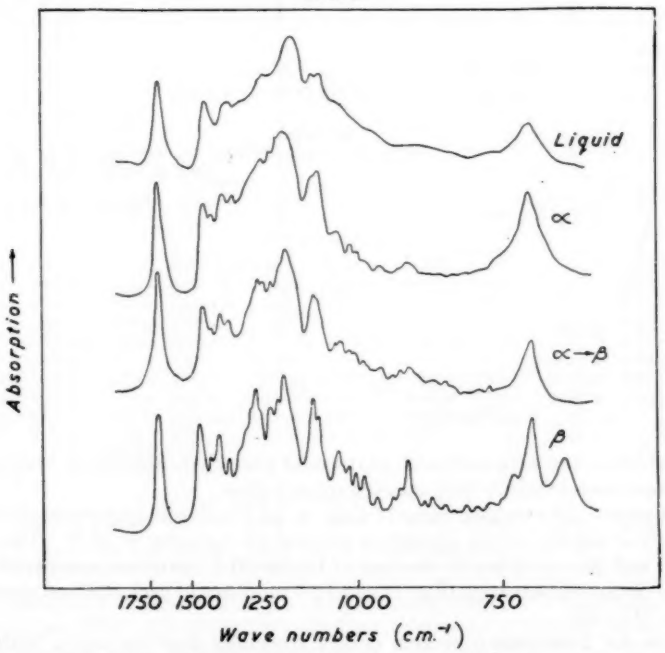


FIG. 4.



FIGS. 3 & 4. *Infrared spectra of polymorphic forms of* (*Fig.* 3) *cocoa butter and* (*Fig.* 4) *mixture* A.

FIG. 5.

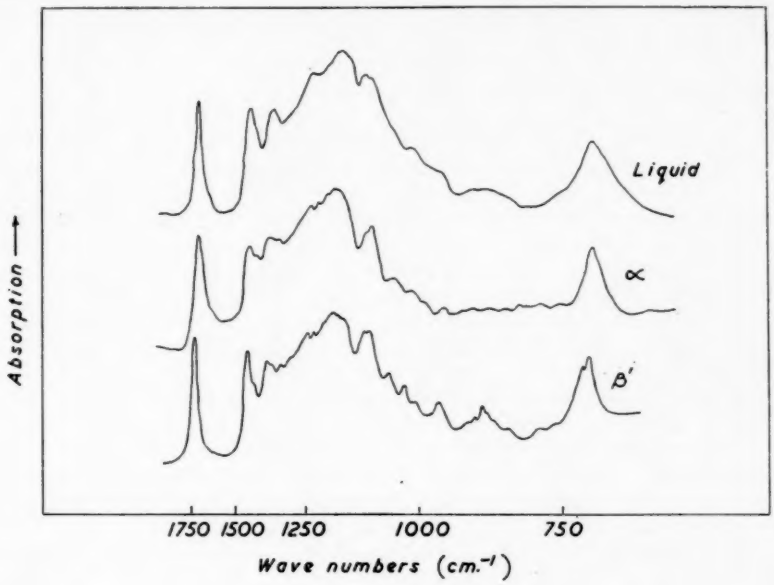
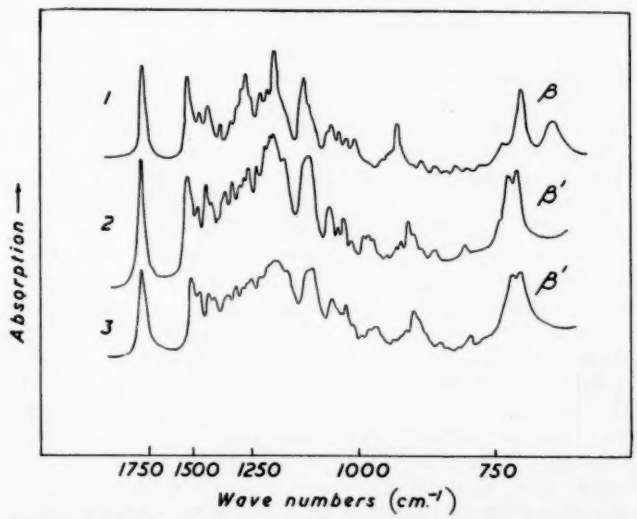


FIG. 6.



FIGS. 5 & 6. *Infrared spectra of* (*Fig.* 5) *polymorphic forms of mixture* B, *and* (*Fig.* 6) (1) 2-*oleopalmitostearin*, (2) 2-*palmito-oleostearin*, *and* (3) *a lard fraction.*

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2-palmito-oleostearin are characteristically different. This is a strong indication of the presence, in cocoa butter, of the 2-oleo-isomer; it is confirmed by the cooling curves of 1 : 1 mixtures of the three glycerides with cocoa butter (Fig. 2). The inflexion in the curve of 2-stearo-oleopalmitin is magnified when this glyceride is mixed with cocoa butter; and the mixture containing 2-palmito-oleostearin has a smaller rise of temperature after supercooling than has cocoa butter. In the latter case, although the curve superficially resembles that for cocoa butter, this mixture is characteristically different from cocoa butter and the other 1 : 1 mixtures, in remaining semiliquid and stirrable for a considerable time (57 min.) after the maximum temperature has been reached. The curve for 2-oleo-palmitostearin, however, is similar to that of cocoa butter and the cocoa butter fraction, again indicating the presence of the 2-oleo-isomer. In order to confirm that the remaining glycerides of cocoa butter do not alter the character of the cooling curve of the 2-oleo-compound, the cooling curve for synthetic mixture A (containing the liquid glycerides o cocoa butter) was determined (Fig. 2) : it is also similar to that for cocoa butter.

The cooling curve of the lard fraction . I value 35·0, which is known to contain a preponderance of one of the isomers of oleopalmitostearin, is unlike that for cocoa butter and is very similar to the curve for 2-palmito-oleostearin.

X-Ray Investigation.—Cocoa butter is known to exhibit polymorphism. An *X*-ray powder photograph of cocoa butter in its most stable form gave a pattern analogous to that obtained with pure 2-oleotriglycerides in their most stable form (designated β-3 for the pure glycerides investigated by Lutton [20]). The pure 1-oleotriglycerides have a different *X*-ray pattern and stable form (designated β′-3 by Lutton). This evidence alone suggests that the major glyceride in cocoa butter is the 2-oleo-isomer.

The *X*-ray patterns (see Table) of cocoa butter, the cocoa butter fraction, and of the synthetic mixtures containing the 2-oleo-isomer, are very similar to each other and also resemble that of the pure 2-oleo-isomer. There is little or no resemblance to the patterns of the 2-stearo- or 2-palmito-glycerides, or of synthetic mixtures containing these glycerides.

Infrared Spectroscopic Investigation.—Chapman [21] showed that the polymorphic forms of glycerides and natural fats can be characterised by their spectra, and that, as well as being indicative of a particular polymorphic form, the spectra can also provide information on the chain length and the molecular groupings present. The infrared spectra of some of our materials, in various polymorphic forms, are shown in Figs. 3—5. The spectrum of the most stable polymorphic form (a β′-form) of mixture B differs from the spectra of cocoa butter. The spectra of mixture C (containing the 2-stearo-isomer as the predominant glyceride) are not shown but were also dissimilar from those of cocoa butter. The spectra of mixtures D and E (containing no liquid glycerides) were similar to those of mixtures A and B respectively.

It is of interest that the spectrum of cocoa butter in its most stable crystalline form is very similar to that of the pure 2-oleo-isomer in its β-3 form. (The spectra of the pure glycerides will be described elsewhere.)

The infrared spectrum of the stable polymorphic form of a lard fraction is shown in Fig. 6 : in contrast with that of cocoa butter, it is very similar to that of the 2-palmito-isomer in its stable crystalline form, consistently with the conclusions of Meara [6] and of Quimby *et al.*[7] that the oleodisaturated glycerides of lard consist mainly of this glyceride.

The results from the three methods, *viz.*, cooling curves, *X*-rays, and infrared spectroscopy, show that the main glyceride present in cocoa butter is 2-oleopalmitostearin, and not 2-palmito-oleostearin as previously suggested. In fact 2-palmito-oleostearin has been shown to be the main disaturated glyceride present in lard.

This work has shown the desirability of using several independent analytical methods, in order to arrive at a definite conclusion regarding glyceride configuration. The difficulties of structural analysis of glycerides, as pointed out by Hilditch,[22] mainly occur in the

[21] Chapman, *J.*, 1956, **55**; VIth Internat. Spectroscopic Colloquium, Amsterdam, 1956.
[22] Hilditch, "The Constitution of the Natural Fats," Chapman and Hall, London, 1956.

isolation of pure glycerides from natural fats. However, much information may be gained by application of the techniques, described in the present paper, to concentrates of glycerides and of their hydrogenated products, obtained by low-temperature crystallisation or by other means. By these methods it should also be possible to determine the structures of many other natural fats, as of the minor constituent glycerides of cocoa butter and of the diunsaturated glycerides of lard.

RESEARCH DEPARTMENT, UNILEVER LTD.,
PORT SUNLIGHT, CHESHIRE.

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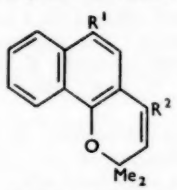
289. *The Reaction between Lapachenole and 2 : 4-Dinitrophenylhydrazine.*

By R. LIVINGSTONE and R. B. WATSON.

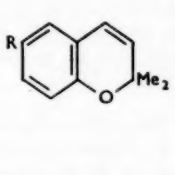
This reaction has been shown to result in the formation of the 2 : 4-dinitrophenylhydrazone of the corresponding 2 : 2-dimethylchromanone and has been extended to related naphthopyrans and chromens.

LAPACHENOLE [1] (I*a*) with 2 : 4-dinitrophenylhydrazine in ethanolic or butanolic sulphuric acid yielded a product formed by the addition of 1 mol. of lapachenole and 1 mol. of 2 : 4-dinitrophenylhydrazine.[2] Lapachenole dimer [1] under similar conditions did not afford a derivative, but 6 : 6-dimethylnaphtho(1′ : 2′-2 : 3)pyran (I*b*) slowly formed a derivative in ethanolic solution. 4′-Chloro-6 : 6-dimethylnaphtho(1′ : 2′-2 : 3)pyran (I*c*) and 2 : 2-dimethylchromen [3] (II*a*) failed to react in ethanol but formed derivatives in refluxing butanol. Dimerisation of lapachenole results in the disappearance of the non-aromatic double bond, indicating that it is probably involved in this " abnormal " reaction with 2 : 4-dinitrophenylhydrazine.

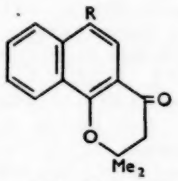
The derivative from 6 : 6-dimethylnaphtho(1′ : 2′-2 : 3)pyran was resistant to hydrolysis with dilute acid and to decomposition by pyruvic acid. It was insoluble in sodium hydroxide or sodium hydrogen carbonate solution, but soluble in chloroform or pyridine. These solubilities, coupled with the fact that the derivative could be eluted from alumina with organic solvents, suggested a cyclic structure.



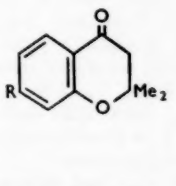
(I) (*a*) $R^1 = OCH_3$, $R^2 = H$. (*b*) $R^1 = H$, $R^2 = H$. (*c*) $R^1 = Cl$, $R^2 = H$. (*d*) $R^1 = H$, $R^2 = CH_3$.



(II) (*a*) $R^1 = H$. (*b*) $R^1 = OCH_3$.



(III) (*a*) R = H. (*b*) $R = OCH_3$.



(IV) (*a*) $R = OCH_3$. (*b*) R = H.

The product was not the 2 : 4-dinitrophenylhydrazone of 1-hydroxy-2-*iso*valerylnaphthalene, obtained by an extension of the method involving Fries re-arrangement of α-naphthol esters.[4] The absence of the hydroxyl group in the " abnormal " compound was confirmed by infrared spectroscopy. The cyclic structure was shown to be of the chromanone type by extending the reaction to 7-methoxy-2 : 2-dimethylchromen in

[1] Livingstone and Whiting, *J.*, 1955, **3631**.
[2] D. H. R. Barton, personal communication.
[3] Shriner and Sharp, *J. Org. Chem.*, 1939, **4**, 575; Smith and Ruoff, *J. Amer. Chem. Soc.*, 1940, **62**, 145.
[4] Stroughton, *ibid.*, 1935, **57**, 202.

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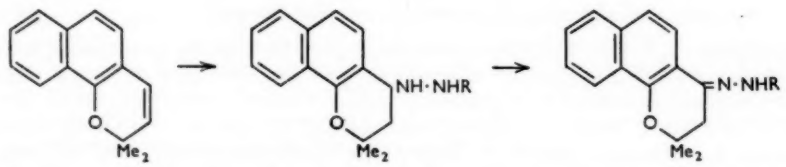
butanol, which afforded the 2 : 4-dinitrophenylhydrazone of 7-methoxy-2 : 2-dimethylchroman-4-one [5] (IV*a*).

The 2 : 4-dinitrophenylhydrazones of 2 : 2-dimethyl-7 : 8-benzochroman-4-one (III*a*), its 6-methoxy-derivative [6] (III*b*), and 2 : 2-dimethylchroman-4-one [7] (IV*b*) were also shown to be identical with the products obtained as above from (I*b*), lapachenole, and (II*a*). The authentic specimens were prepared by the Fries re-arrangement of ββ-dimethylacryloyl esters.[8]

The reaction could be regarded as involving dehydrogenation of the addition product (see scheme), a reaction comparable with the dehydrogenation of alcohol by excess of 2 : 4-dinitrophenylhydrazine.[9] Such a mechanism would explain the fact that 7-methoxy-2 : 2-dimethylchromen and phenylhydrazine in butanolic sulphuric acid failed to yield any derivative. 4 : 6 : 6-Trimethylnaphtho(1′ : 2′-2 : 3)pyran (I*d*) with 2 : 4-dinitrophenylhydrazine in butanol also failed to yield a derivative, the elimination of the methyl group being difficult to envisage under the conditions of the reaction. Presumably the addition step is reversible and unless dehydrogenation supervenes the adduct reverts to its precursors.



6-Methoxy-2 : 2-dimethylchromen (II*b*) showed a lower reactivity than its 7-methoxy-analogue, and 2 : 2-diphenyl-1 : 2-benzopyran [10] failed to yield any derivative when heated under reflux with 2 : 4-dinitrophenylhydrazine in butanolic sulphuric acid.

Experimental

Ultraviolet absorption spectra were determined in $CHCl_3$ with a Unicam S.P.500 spectrophotometer.

Lapachenole 2 : 4-Dinitrophenylhydrazine Derivative.—Lapachenole (0·5 g.), 2 : 4-dinitrophenylhydrazine (1 g.), ethanol (100 c.c.), and sulphuric acid (2 c.c.) were refluxed for 1 hr. and the precipitate purified by chromatography on alumina from benzene. The *product* (see below) separated from acetic acid in red-brown needles, m. p. 293—296° (Found: C, 59·95; H, 4·45; N, 12·45; OMe, 7·1. $C_{22}H_{20}O_6N_4$ requires C, 60·5; H, 4·6; N, 12·8; OMe, 7·1%), $\lambda_{max.}$ 2460, 3320, 4250 Å (log ε 4·39, 4·12, 4·43).

6 : 6-*Dimethylnaphtho*(1′ : 2′-2 : 3)*pyran* 2 : 4-*Dinitrophenylhydrazine Derivative.*—6 : 6-Dimethylnaphtho(1′ : 2′-2 : 3)pyran (I*b*) (0·9 g.), 2 : 4-dinitrophenylhydrazine (1 g.), ethanol (100 c.c.), and sulphuric acid (2 c.c.) was refluxed for 3½ hr., then set aside overnight. The precipitated *product* was purified by chromatography on alumina from benzene. Crystallisation from acetic acid afforded needles, m. p. 279—280° (0·12 g., 7%) (Found: C, 62·4; H, 4·25; N, 13·75. $C_{21}H_{18}O_5N_4$ requires C, 62·1; H, 4·5; N, 13·8%), $\lambda_{max.}$ 3100 and 4050 Å (log ε 3·96, 4·44).

Reaction of 2 : 4-Dinitrophenylhydrazine and 2 : 2-Dimethylchromens in Butanol.—Dimethylchromen (1 mole), 2 : 4-dinitrophenylhydrazine (2·2 moles), butan-1-ol (3·5 l./mole), and sulphuric acid (0·38 l./mole) were refluxed for 3 hr. The residue afforded by the removal of solvent and excess of hydrazine was purified by chromatography on alumina from benzene. The derivative was recrystallised from a suitable solvent.

[5] Bridge, Crocker, Cubin, and Robertson, *J.*, 1937, 1530.
[6] Livingstone and Watson, *ibid.*, *J.*, 1956, 3701.
[7] Baker, Floyd, McOmie, Pope, Weaving, and Wild, *J.*, 1956, 2015.
[8] Cavill, Dean, McGookin, Marshall, and Robertson, *J.*, 1954, 4173.
[9] Braude and Forbes, *J.*, 1951, 1762.
[10] Löwenbein, *Ber.*, 1924, **75**, 779.

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(a) 2 : 2-*Dimethylchromen* (II*a*). The product, obtained as reddish needles from benzene and then from ethyl acetate, had m. p. 215—216° alone or mixed with 2 : 2-dimethylchroman-4-one 2 : 4-dinitrophenylhydrazone.[7]

(b) 6-*Methoxy*-2 : 2-*dimethylchromen* (II*b*). The *derivative* obtained as orange-red needles from benzene had m. p. 199—207° (5%) (Found : C, 56·1; H, 4·8; N, 14·1. $C_{18}H_{18}O_6N_4$ requires C, 56·0; H, 4·7; N, 14·5%).

(c) 7-*Methoxy*-2 : 2-*dimethylchromen*. A derivative obtained as blood-red needles from benzene and then from ethyl acetate had m. p. 219—220° (10%) alone or mixed with 7-methoxy-2 : 2-dimethylchroman-4-one 2 : 4-dinitrophenylhydrazone [5] (Found : C, 55·6; H, 4·7; N, 14·4. Calc. for $C_{18}H_{18}O_6N_4$: C, 56·0; H, 4·8; N, 14·4%).

(d) 4′-*Chloro*-6 : 6-*dimethylnaphtho*(1′ : 2′-2 : 3)*pyran* (I*c*). A solid, which separated from the solution during the heating, was purified separately from the residue. The *product* was obtained as orange-red plates (from benzene), m. p. 281—282° (Found : C, 56·8; H, 4·0; N, 12·6; Cl, 7·4. $C_{21}H_{17}O_5N_4Cl$ requires C, 57·2; H, 4·0; N, 12·7; Cl, 8·0%).

6-*Methoxy*-2 : 2-*dimethyl*-7 : 8-*benzochroman*-4-*one* 2 : 4-*Dinitrophenylhydrazone*.—The crude derivative, obtained by treating a warm ethanolic solution of 6-methoxy-2 : 2-dimethyl-7 : 8-benzochroman-4-one [6] with an excess of Brady's reagent, was purified by chromatography on alumina from benzene. Crystallisation from benzene afforded carmine plates, m. p. 292—293° (decomp.) alone or mixed with the 2 : 4-dinitrophenylhydrazone product from lapachenole (Found : C, 59·95; Cl, 4·45; N, 13·05%).

1-*Naphthyl* ββ-*Dimethylacrylate*.—α-Naphthol (5·25 g.), 3-methylbut-2-enoyl chloride (3·5 c.c.), and magnesium were refluxed in benzene (30 c.c.) for 1 hr., yielding the *ester*, b. p. 191—194°/13 mm., yellow prisms, m. p. 46—47° (4·33 g.) (Found : C, 79·5; H, 5·9. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%).

2 : 2-*Dimethyl*-7 : 8-*benzochroman*-4-*one*.—Naphthyl ββ-dimethylacrylate (4·3 g.) and aluminium chloride (4·5 g.) were heated together at 140—150° for 2½ hr. and after acidic decomposition and ether-extraction furnished a yellow oil, b. p. 172—184°/2 mm. (1·25 g.). The distillate was refluxed in ethanol (25 c.c.) and 3% hydrochloric acid (15 c.c.) for 24 hr. After evaporation of solvent, the residue was saturated with ammonium sulphate. The product was isolated with ether and chromatographed on alumina from benzene, affording the *chromanone* as a viscous oil (0·77 g.) (Found : C, 79·5; H, 5·9. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%). Its 2 : 4-dinitrophenylhydrazone formed red needles (from benzene), m. p. 279—280°, alone or mixed with the 6 : 6-dimethylnaphtho(1′ : 2′-2 : 3)pyran 2 : 4-dinitrophenylhydrazine derivative (Found : N, 13·75%).

1-*Hydroxy*-2-iso*valerylnaphthalene*.—α-Naphthol (14·4 g.) and *iso*valeryl chloride (13 c.c.), when refluxed for 1 hr., afforded 1-*naphthyl* iso*valerate*, b. p. 178°/12 mm. (10 g.) (Found : C, 79·1; H, 7·3. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·1%), which (10 g.) was heated with aluminium chloride (10 g.) for 2 hr. at 100° and then for 1 hr. at 120°. After decomposition with dilute acid and steam-distillation, the product was extracted with ether from the distillate. Evaporation and crystallisation from aqueous ethanol yielded 1-hydroxy-2-*iso*valerylnaphthalene as pale yellow needles, m. p. 63—64° (lit.,[11] m. p. 64—65°) (Found : C, 79·1; H, 7·3. Calc. for $C_{15}H_{16}O_2$: C, 78·9; H, 7·1%). The 2 : 4-*dinitrophenylhydrazone* crystallised from nitrobenzene as red needles, m. p. 242—244° (decomp.) (Found : N, 13·3. $C_{21}H_{20}O_5N_4$ requires N, 13·7%).

Preparation of Dimethylchromens and Dimethylnaphthopyrans.—The coumarin (0·05 mole) in dry benzene (200 c.c.) was added slowly (1¼ hr.) to a stirred Grignard solution from methyl iodide (0·17 mole), magnesium (0·17 g.-atom), and ether (50 c.c.). The solution was refluxed for 1 hr. and set aside overnight. Decomposition with 22% ammonium chloride solution (150 c.c.) and extraction with ether gave an ethereal solution, which was washed with water and dried ($CaCl_2$). Removal of solvent and distillation gave the chromens and naphthopyrans. Picrates were prepared from methanolic solutions of the components.

6 : 6-*Dimethylnaphtho*(1′ : 2′-2 : 3)*pyran* (I*b*) (from 7 : 8-benzocoumarin [12]), b. p. 172—176°/15 mm. (55%) (Found : C, 85·5; H, 7·0. $C_{15}H_{14}O$ requires C, 85·7; H, 6·7%), gave a *picrate*, red needles, m. p. 123—125° (Found : N, 9·6. $C_{21}H_{17}O_8N_3$ requires N, 9·6%).

4 : 6 : 6-*Trimethylnaphtho*(1′ : 2′-2 : 3)*pyran* (I*d*) (from 4-methyl-7 : 8-benzocoumarin [13]), b. p. 182—184°/15 mm. (75%) (Found : C, 85·95; H, 7·4. $C_{16}H_{16}O$ requires C, 85·7;

[11] Yuoh-Fong Chi and Cherng-Tsum Jung, *J. Amer. Chem. Soc.*, 1941, **63**, 3155.
[12] Dey, Rao, and Sankaranarayanan, *J. Indian Chem. Soc.*, 1932, **9**, 71.

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H, 7·2%), gave a *picrate*, dark-red needles, m. p. 124—125° (Found: N, 9·2. $C_{22}H_{19}O_8N_3$ requires N, 9·3%).

4'-Chloro-6 : 6-dimethylnaphtho(1' : 2' : 2 : 3)*pyran* (Ic) (from 6-chloro-7 : 8-benzocoumarin [14]) had b. p. 168—170°/15 mm., m. p. 52—54° (33%) (Found: C, 73·2; H, 5·9; Cl, 13·7. $C_{15}H_{13}OCl$ requires C, 73·6; H, 5·4; Cl, 14·5%).

7-Methoxy-2 : 2-dimethylchromen (from 7-methoxycoumarin [5]) had b. p. 140—141°/16 mm., n_D^{21} 1·5548 (44%) (Found: C, 75·4; H, 7·2. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%).

6-Methoxy-2 : 2-dimethylchromen (IIb) (from 6-methoxycoumarin [15]) had b. p. 132—136°/15 mm., n_D^{19} 1·5558 (47%) (Found: C, 75·3; H, 7·1%).

We thank Professor D. H. R. Barton, F.R.S., for the sample of lapachenole 2 : 4-dinitrophenylhydrazone and his preliminary results, Dr. M. C. Whiting for advice and interest, Professor E. R. H. Jones, F.R.S., for the provision of facilities for some microanalyses and infrared spectroscopy at the University of Manchester, and Dr. G. R. Ramage for provision of facilities for ultraviolet spectroscopy at Huddersfield Technical College. One of us (R. B. W.) acknowledges financial assistance from Burnley Education Authority.

MUNICIPAL COLLEGE, BURNLEY. [*Received, August 20th*, 1956.]

[13] Henry, Sandrock, and Robertson, *J.*, 1931, 2426.
[14] Chakravarti and Bagchi, *J. Indian Chem. Soc.*, 1936, **13**, 649.
[15] Ferd, Tiemann, and Muller, *Ber.*, 1881, **14**, 1996.

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290. *A New Sequence for the Conversion of an Aromatic Aldehyde into the Next Higher Acid. A New Synthesis of* m-*Nitrophenylacetic Acid.*

By K. F. JENNINGS.

m-Nitrobenzaldehyde has been converted into 2-methyl-4-*m*-nitrobenzylideneoxazolone, which on mild treatment with hydrazine hydrate gave α-acetamido-*m*-nitrocinnamhydrazide. This, on diazotisation, produced the azide, which in boiling benzene gave 3 : 4-dihydro-6-methyl-4-*m*-nitrobenzylidene-2-oxo-1 : 3 : 5-oxadiazine. Hydrolysis of the last compound gave *m*-nitrophenylacetic acid. The overall yield was 31%. α-Acetamido- and α-benzamido-*m*-nitrocinnamhydrazide, upon digestion with acetic anhydride–acetic acid, gave partly reduced 1 : 2 : 4-triazines, whose structures were not fully established. The latter on alkaline hydrolysis gave α-benzamido-*m*-nitrocinnamic acid quantitatively. Aceturhydrazide yielded *N*-aceturyl-*N'*-acetylhydrazine.

THAT 4-*m*-nitrobenzylideneoxazolones cannot be hydrolysed to α-oxo-acids is well known,[1] and the same is true for the rhodanines. Hence, attention was directed to the possible hydrolysis products of the oxadiazine derivatives (IV) obtained from the azides (III) of α-substituted amino-hydrazides (II), which in turn are derivable from oxazolones (I).[2]

As models, the azlactones obtained from *m*-nitrobenzaldehyde were examined. 2-Methyl-4-*m*-nitrobenzylideneoxazolone (I; R = Me) on treatment with hydrazine hydrate, in ethanol, at room temperature, gave α-acetamido-*m*-nitrocinnamhydrazide (II; R = Me), which with one equivalent of nitrous acid yielded α-acetamido-*m*-nitrocinnamoyl azide (III; R = Me). Azides of this type may undergo various transformations; in cold pyridine or boiling ethanol they are converted into the parent oxazolone, whereas in hot benzene or toluene partly saturated 2-oxo-1 : 3 : 5-oxadiazines result. The azides may be recrystallised (although in this series, badly) from acetone. As expected,

[1] Burton, *J.*, 1935, 1265; cf. Jennings, *J.*, 1957, 1172.
[2] Clarke, Johnson, and Robinson, "The Chemistry of Penicillin," Princeton Univ. Press, 1949, p. 735.

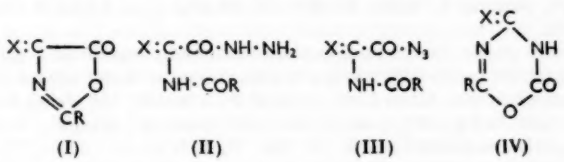
the compound (III; R = Me) in boiling benzene gave **3 : 4-dihydro-6-methyl-4-*m*-nitrobenzylidene-2-oxo-1 : 3 : 5-oxadiazine** (IV; R = Me), presumably *via* an *iso*cyanate. On digestion with warm aqueous sodium hydroxide, this gave a very low yield of *m*-nitrophenylacetic acid, but acid hydrolysis gave the same product quantitatively. The overall yield from *m*-nitrobenzaldehyde was 31%.

For comparison, the phenyl analogues (I, II, III, and IV; R = Ph) were prepared in a similar manner. In the case of α-benzamido-*m*-nitrocinnamhydrazide (II; R = Ph) *cis*- and *trans*-isomers were isolated, the latter greatly predominating. Presumably, the phenyl analogue (IV; R = Ph) on similar acid hydrolysis gave the desired product and benzoic acid, but as these have the same m. p. and parallel solubilities in water, separation was not accomplished. However, the yield of **3 : 4-dihydro-4-*m*-nitrobenzylidene-2-oxo-6-phenyl-1 : 3 : 5-oxadiazine** (IV; R = Ph) from *m*-nitrobenzaldehyde was 42%, which contrasts favourably with the methyl series.

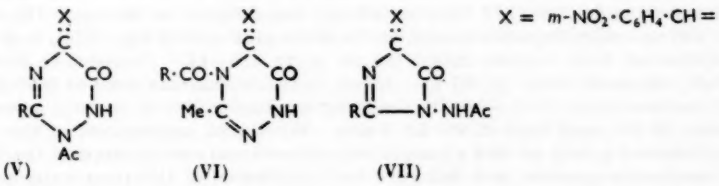
Hence, a new route from an aromatic aldehyde to the arylacetic acid is announced. It offers the advantage over the Erlenmeyer azlactone synthesis in that a nitro-group attached to the aromatic (or principal aromatic) residue in the *meta* position does not prevent it. Although twice as many steps from the oxazolone are needed, they are rapid and easy.

Treatment of α-acetamido-*m*-nitrocinnamhydrazide with hot acetic anhydride–acetic acid gave the triazine derivative (V) or (VI) (R = Me),[3] depending upon the reactivities of the carbonyl group of the acetylhydrazino- or amido-residue. Undoubtedly, acetylation is the first step. *trans*-α-Benzamido-*m*-nitrocinnamhydrazide similarly yielded either (V) or (VI) (R = Ph).

It is yet possible that the acetamidohydrazide (II; R = Me) may have afforded the triazine (V; R = Me), and the benzamidohydrazide (II; R = Ph) the triazine (VI; R = Ph), or *vice versa*. These classes of compounds are new.



(I) (II) (III) (IV)



(V) (VI) (VII)

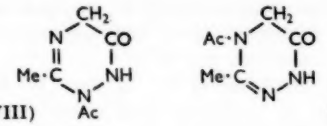
An alternative possibility of cyclisation to the glyoxaline derivative (VII) is discounted, since the compound (V or VI; R = Ph) on digestion with aqueous alkali gave a quantitative yield of α-benzamido-*m*-nitrocinnamic acid, while (V or VI; R = Me) in similar circumstances produced a tar. The glyoxaline ring would be stable under these conditions.

Presumably, another product from the hydrolysis of (V or VI; R = Ph) would be acethydrazide, since α-benzamidocinnamhydrazide with alkali gave 5-benzyl-6-hydroxy-3-phenyl-1 : 2 : 4-triazine.[4] Had α-acetamido- and α-benzamido-*m*-nitrocinnamhydrazide yielded simple acetyl derivatives, these upon digestion with alkali might have been expected

[3] Cf. Vanghelovici and Stefanescu, *Soc. Chim. România, Sect. Soc. române Stiinte, Bul. Chim. pură Apl.*, 1941—42, [2], **3**, *A*, 159; *Chem. Abs.*, 1944, **38**, 5501.

[4] Ref. 2, p. 736.

to produce 6-hydroxy-3-methyl-5-nitrobenzyl-1 : 2 : 4-triazine and its 3-phenyl analogue respectively.



(VIII) (IX)

An attempt to prepare the *pseudo*-parent compound (VIII) or (IX) from aceturhydrazide gave only a low yield of two crystalline forms of *N*-aceturyl-*N'*-acetylhydrazine. This is somewhat surprising in view of the ready cyclisations reported above, and the presumed ring closure of aceturic acid in the Erlenmeyer azlactone synthesis.

Experimental

M. p.s are corrected.

2-Methyl-4-m-nitrobenzylideneoxazolone.—*m*-Nitrobenzaldehyde (15·1 g.), fused sodium acetate (16·4 g.), aceturic acid (11·1 g.), and acetic anhydride (31 g.) were heated in a boiling-water bath for 3 hr., the mixture setting to a yellow solid. Water (50 ml.) was added and, when cool, the cake was filtered off and washed with hot water and cold ethanol. *2-Methyl-4-m-nitrobenzylideneoxazolone* (18·5 g., 80%) had m. p. 156—157°. Recrystallisation from acetone–ethanol gave bright yellow needles of unchanged m. p. (Found: N, 11·8. $C_{11}H_8O_4N_2$ requires N, 12·1%). In EtOH it has one maximum at 3200 Å (ε 15,400).

α-Acetamido-m-nitrocinnamhydrazide.—2-Methyl-4-*m*-nitrobenzylideneoxazolone (1·85 g.) was mixed with a solution of 100% hydrazine hydrate (1·0 g.) in ethanol (9 ml.), the deep yellow colour of the oxazolone immediately changing to the light yellow of the product, which was filtered off, washed with ethanol, and dried. *α-Acetamido-m-nitrocinnamhydrazide* (1·55 g., 74%), recrystallised from ethanol, gave long needles, m. p. 160—161° (Found: C, 50·2; H, 4·6; N, 21·0. $C_{11}H_{12}O_4N_4$ requires C, 50·0; H, 4·6; N, 21·2%). In EtOH it has one maximum at 2700 Å (ε 17,200).

α-Acetamido-m-nitrocinnamoyl Azide.—α-Acetamido-*m*-nitrocinnamhydrazide (5·5 g.) was treated in N-hydrochloric acid (60 ml.) with 95% sodium nitrite (2·0 g.) in water (40 ml.), with stirring. The immediate precipitate was filtered off, washed with water, and dried to give *α-acetamido-m-nitrocinnamoyl azide* (5·3 g., 93%), m. p. 100—102° (decomp.) (Found: C, 47·3; H, 3·6; N, 24·4. $C_{11}H_9O_4N_5.\frac{1}{4}H_2O$ requires C, 47·2; H, 3·4; N, 25·0%).

3 : 4-Dihydro-6-methyl-4-m-nitrobenzylidene-2-oxo-1 : 3 : 5-oxadiazine.—α-Acetamido-*m*-nitrocinnamoyl azide (2·0 g.) in benzene (20 ml.) was refluxed for 30 min. The solution was filtered, and on cooling deposited orange needles of the *oxadiazine* (1·0 g., 56%), m. p. 109—110°. Recrystallisation from benzene raised the m. p. to 116—117° (Found: C, 53·9; H, 4·0. $C_{11}H_9O_4N_3$ requires C, 53·4; H, 3·7%). It has, in MeOH, one maximum at 2650 Å (ε 19,600).

m-Nitrophenylacetic Acid.—(*a*) The foregoing oxadiazine (1·5 g.) in 10% aqueous sodium hydroxide (30 ml., and kept at 80° for 5 min. When cool, acidification of the solution by hydrochloric acid gave a tar (0·3 g.) which was removed and concentration of the filtrate gave impure *m*-nitrophenylacetic acid (0·2 g.). Recrystallisation of this from water yielded fawn needles (0·1 g., 9%), m. p. 118·5—119·5° (Found: N, 7·6. Calc. for $C_8H_7O_4N$: N, 7·8%). Salkowski [5] reported m. p. 120°.

(*b*) The oxadiazine (1·55 g.) was heated with 5N-hydrochloric acid (40 ml.) at 80° for 30 min. Upon cooling, the solution gave *m*-nitrophenylacetic acid (0·75 g.), m. p. 117—118°, and concentration of the mother-liquor gave a second crop (0·4 g.) of the same m. p. and mixed m. p. The total yield was 100%.

α-Benzamido-m-nitrocinnamhydrazide.—*4-m*-Nitrobenzylidene-2-phenyloxazolone [6] (11·7 g.) was mixed with ethanol (65 ml.) containing 100% hydrazine hydrate (10·0 g.). After a few minutes, *α-benzamido-m-nitrocinnamhydrazide* (10·0 g., 77%) was filtered off, washed with ether, and dried; it had m. p. 190—191° (Found: C, 59·1; H, 4·1; N, 17·0. $C_{16}H_{14}O_4N_4$ requires C, 58·9; H, 4·3; N, 17·2%). In MeOH, this had maxima at 2300 and 2625 Å (ε 17,000

[5] Salkowski, *Ber.*, 1884, **17**, 506.
[6] Douglas and Gulland, *J.*, 1931, 2893.

and 16,150 respectively), and is probably the *trans*-isomer.[7] Concentration of the ethanolic mother-liquor gave a second crop (0·5 g., 3·5%), m. p. 208—209°, depressed in m. p. on admixture with the above sample. Recrystallisation from ethanol gave needles, m. p. 208—208·5° (Found: C, 59·05; H, 4·0; N, 16·8%). This had, in MeOH, one maximum at 2600 Å (ε 7600) and is probably the cis-*isomer*. In the infrared absorption spectra, the positions of the bands were similar, but not their intensities. Vanghelovici and Stefanescu[3] gave m. p. 195° and an erroneous constitution of this compound.

α-*Benzamido*-m-*nitrocinnamoyl Azide*.—α-Benzamido-*m*-nitrocinnamhydrazide (3·25 g.; m. p. 190—191°), treated in the same way as the acetamido-analogue, gave α-*benzamido*-m-*nitrocinnamoyl azide* (2·95 g., 88%), m. p. 76—77° (Found: C, 53·8; H, 3·5. $C_{16}H_{11}O_4N_5,H_2O$ requires C, 54·1; H, 3·7%). Vanghelovici *et al.*[3] give m. p. 80° (decomp.) and an erroneous formulation. This compound is white when wet with water, and yellow when a monohydrate.

3 : 4-*Dihydro*-4-m-*nitrobenzylidene*-2-*oxo*-6-*phenyl*-1 : 3 : 5-*oxadiazine*.—α-Benzamido-*m*-nitrocinnamoyl azide (2·8 g.) in benzene (56 ml.) was heated at 85—90° for 20 min. There was brisk evolution of nitrogen with precipitation of the product. When cool, the *oxadiazine* (1·7 g., 66%) was filtered off: it had m. p. 185—186·5° (decomp.) (Found: N, 13·4. $C_{16}H_{11}O_4N_3$ requires N, 13·6%). In MeOH, it has maxima at 2550, 2750, 3550, and 3700 Å (ε 13,200, 12,200, 5100, and 5100 respectively).

Treatment of α-*Acetamido*-m-*nitrocinnamhydrazide with Acetic Anhydride–Acetic Acid*.—A solution of α-acetamido-*m*-nitrocinnamhydrazide (1·0 g.) in acetic anhydride (10 ml.) and acetic acid (10 ml.) was heated at 100° for 30 min., and then cooled. Dilution with water (30 ml.) gave a product (0·5 g., 57%) of m. p. 215—216°. Recrystallisation from ethanol gave light yellow microcrystals of unchanged m. p. (Found: C, 54·0, 53·7; H, 4·4, 4·2; N, 19·8; *C*-Me, 18·6. $C_{13}H_{12}O_4N_4$ requires C, 54·2; H, 4·2; N, 19·45; *C*-Me, 18·7%). In Nujol, the principal bands of this compound are at 2·99 (>NH), 5·79 (cyclic lactam), 5·94 (>NAc), 6·03 (conjugated C:N), and 6·54 μ (bending >NH); and in MeOH, it has maxima at 2450, 2750, and 3400 Å (ε 9500, 12,300, and 16,500 respectively). It is formulated, therefore, as either 2-*acetyl*-1 : 2 : 5 : 6-*tetrahydro*-3-*methyl*-5-m-*nitrobenzylidene*-6-*oxo*-1 : 2 : 4-*triazine* or 4-*acetyl*-1 : 4 : 5 : 6-*tetrahydro*-3-*methyl*-5-m-*nitrobenzylidene*-6-*oxo*-1 : 2 : 4-*triazine*.

Treatment of α-*Benzamido*-m-*nitrocinnamhydrazide with Acetic Anhydride–Acetic Acid*.—A solution of α-benzamido-*m*-nitrocinnamhydrazide (4·8 g; m. p. 190—191°) in acetic anhydride (70 ml.) and acetic acid (70 ml.) was heated at 100° for 40 min. After filtration and dilution with water (100 ml.), the product (3·4 g., 66%) was recrystallised from ethanol–water and gave needles, m. p. 199—201° (Found: C, 59·1; H, 4·6; N, 14·7. $C_{18}H_{14}O_4N_4,H_2O$ requires C, 58·7; H, 4·4; N, 15·2%). The principal infrared absorption bands (in Nujol) are at 3·08 (>NH), 5·75 (weak, undesignated), 5·98 (conjugated >CO), 6·04 (amide), 6·55 μ; (secondary amide); and in MeOH it has maxima at 2300, 2675, and 3600 Å (ε 12,700, 12,200, and 1870 respectively). This product is probably 2-*acetyl*-1 : 2 : 5 : 6-*tetrahydro*-6-*oxo*-5-m-*nitrobenzylidene*-3-*phenyl*-1 : 2 : 4-*triazine* or 4-*benzoyl*-1 : 2 : 5 : 6-*tetrahydro*-3-*methyl*-5-m-*nitrobenzylidene*-6-*oxo*-1 : 2 : 4-*triazine*.

α-*Benzamido*-m-*nitrocinnamic Acid*.—(*a*) The product (0·7 g.) obtained as described immediately above, was heated with 10% aqueous sodium hydroxide (*ca.* 10 ml.) until dissolved (*ca.* 1 min. at 100°). The dark red solution was cooled and acidified to Congo-red by hydrochloric acid, and the pink precipitate was collected, washed, and dried, to give α-benzamido-*m*-nitrocinnamic acid (0·6 g., 100%), m. p. 220—222°. Recrystallisation from acetone–benzene raised the m. p. to 230—231° (Found: C, 61·1; H, 4·1; N, 9·35. Calc. for $C_{16}H_{12}O_5N_2$: C, 61·5; H, 3·85; N, 9·0%). In EtOH, the acid has maxima at 2250 and 2650 Å (ε 30,300 and 23,200 respectively).

(*b*) 4-*m*-Nitrobenzylidene-2-phenyloxazolone[8] (2·0 g.) was heated at 100° with 10% aqueous sodium hydroxide (20 ml.) for 5 min. (*i.e.*, until homogeneous), cooled, and made acid to Congo-red by hydrochloric acid. The precipitate (1·4 g., 66%) had m. p. 222—223°, undepressed on admixture with the above sample. Douglas and Gulland,[8] in a preparation requiring 4 days, obtained a product of m. p. 223—224°.

N-*Aceturyl*-N'-*acetylhydrazine*.—Aceturhydrazide[9] (1·35 g.) was heated in 1 : 1 acetic

[7] Cf. Gillam and Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Arnold, London, 1954, p. 232.
[8] Ref. 6, p. 2902.
[9] Radenhausen, *J. prakt. Chem.*, 1895, **52**, 442.

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anhydride–glacial acetic acid (20 ml.) at 100° for 30 min. Removal of the solvents *in vacuo* gave a yellow oil, which, from methanol, yielded N-*aceturyl*-N'-*acetylhydrazine* (0·05 g., 3%) as small granules of m. p. 220° (decomp.) (Found: C, 41·4; H, 6·3. $C_6H_{11}O_3N_3$ requires C, 41·6; H, 6·4%). By dilution of the methanolic solution with ether, there was obtained a second crop (0·3 g., 17%), m. p. 181·5—182° (Found: C, 41·6; H, 6·4%). This compound is very water-soluble.

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DYSON PERRINS LABORATORY, SOUTH PARKS ROAD, OXFORD.
[Present address: DEFENCE RESEARCH CHEMICAL LABORATORIES, OTTAWA, CANADA.]
[*Received, August 24th*, 1956.]

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291. *Addition Compounds of Gallium Trichloride. Part II.*[1] *Gallium Trichloride–Phosphorus Oxychloride.*

By N. N. GREENWOOD and K. WADE.

The melting-point diagram of the system gallium trichloride–phosphorus oxychloride shows the presence of a new compound, $GaCl_3,POCl_3$, m. p. 118·5°, and the possible formation of a second compound $GaCl_3,2POCl_3$ melting incongruently at about 77°. The 1 : 1 compound has a vapour pressure of <1 mm. at the melting point and can be sublimed *in vacuo* without decomposition. The specific electrical conductivity, viscosity, density, and surface tension of the molten compound have been determined over a range of temperature in order to calculate the molar conductivity, reduced conductivity, activation energy of conduction, activation energy of viscous flow, molar surface free energy, parachor, and related properties. Direct-current current–voltage experiments have also been carried out. It is suggested that chlorine rather than oxygen is the donor atom and that the complex is dissociated to the extent of about ½% into the ions $POCl_2^+$ and $GaCl_4^-$. The results are compared with those obtained on other systems in which phosphorus oxychloride is the ligand.

PHYSICAL properties of the new compound gallium trichloride–phosphorus oxychloride, which is formed rapidly and exothermally by gallium trichloride in the presence of phosphorus oxychloride vapour, are reported. The complex melts to give a stable liquid of moderately high electrical conductivity and is ideally suited to physicochemical studies. Its properties are compared with those of other gallium trichloride addition compounds and with other complexes in which phosphorus oxychloride is the ligand. It is considered to ionise as $POCl_2^+GaCl_4^-$.

EXPERIMENTAL AND RESULTS

Gallium trichloride was prepared and purified as described in Part I.[1] Phosphorus oxychloride was fractionated in an efficient column and then vacuum distilled. Mixtures of known composition for the phase diagram were prepared by the techniques used for the system with acetyl chloride.[1] Gallium trichloride absorbed phosphorus oxychloride spontaneously and with considerable evolution of heat up to 49 moles % of $POCl_3$; thereafter, further phosphorus oxychloride was condensed from the vacuum line by cooling the reaction vessel in alcohol–solid carbon dioxide. There was a slight initial attack on the Apiezon M tap grease but this had no apparent effect on the results.

Pure gallium trichloride–phosphorus oxychloride was prepared on the 50 g. scale by absorbing the required weight of phosphorus oxychloride *in vacuo* on a known weight of resublimed gallium trichloride at *ca.* 120°. The compound which had the correct composition to within 1 part in 8000 by weight, was a white solid which melted to a clear, colourless liquid.

[1] Part I, Greenwood and Wade, *J.*, 1956, 1527.

The electrical conductivity of the molten compound was measured at 1000 c./sec. with the circuit previously described.[2] The cell, shown in Fig. 1, was of soda-glass with platinum electrodes sealed through sleeves of cobalt glass. The volume to the etched mark was 9·5 ml. and the cell constant was 0·9152 cm.$^{-1}$. The resistance, which varied between 500 and 700 ohms, was measured to within 1 part in 3000. The side arms were sealed at atmospheric pressure to restrict the otherwise violent movement of the mercury contacts during handling. A graded seal, *C*, connected the soda-glass cell to the Pyrex-glass loading unit. The complex was sealed into the wide entry tube *A*, the apparatus evacuated through section *D*, and the complex melted, run into the crystallisation bulbs *B* and degassed, after which the apparatus was sealed at points 1 and 2. The remaining central unit was inverted and the compound fractionally crystallised five times by being melted at 125° and cooled at 112°, about one fifth of the solidifying liquid being rejected in each cycle. The m. p. did not rise appreciably during this process and the final purified sample melted at 118·5°. The pure compound was run into the cell for a preliminary conductivity measurement. With the fractionation bulbs outside the thermostat, but still connected to the cell, the conductivity increased slowly by 6% over a period of 8 hr. at 127°, most of this increase occurring during the first 2 hr. The compound was returned to the double-bulb unit and fractionally recrystallised again but the effect persisted: the conductivity, initially close to the first values on the preceding run, increased by 4% in 3½ hr. and 5% in 6½ hr. Further experiments showed that constant values could only be obtained when the cell was sealed off at point 3 and totally immersed in the thermostat. The increase in conductivity in the earlier experiments was presumably due either to the slow irreversible evaporation of one of the components from the complex or, more probably, to the reabsorption *via* the vapour phase of some component initially rejected in the fractional crystallisation. When the conductivity was measured in an isolated, totally immersed cell, it remained constant to within 0·1% during several hours at 127°.

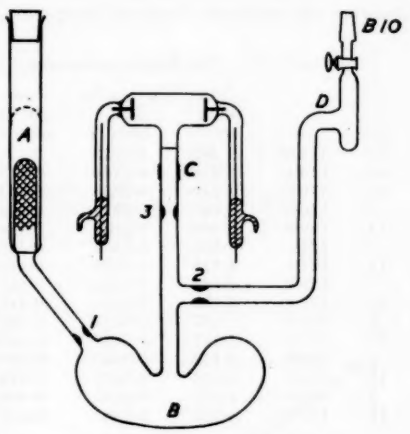

FIG. 1. *Conductivity cell.*

TABLE 1. *Melting point of the system gallium trichloride–phosphorus oxychloride.*

$POCl_3$ (mole %) ...	0·0	2·6	6·2	8·7	11·8	14·2	17·5	21·8	23·8
M. p.	77·8°	76·5°	74°	70°	65°	60°	52° *	36° *	26° *
$POCl_3$ (mole %)	25·0	28·3	31·4	34·3	37·9	39·4	42·1	45·6	49·2
M. p.	18° *	30° *	54° *	68·5° *	83°	87°	96°	107°	117·5°
$POCl_3$ (mole %)	50·8	53·4	58·6	63·1	65·8	68·7	70·7	73·0	76·6
M. p.	117·5°	113°	102°	90°	82°	74°	69°	63°	53°
$POCl_3$ (mole %)	80·0	82·4	84·3	86·0	87·1	88·9	90·9	100·0	
M. p.	42°	33° †	23° †	15° †	9° †	−1° †	−3° †	+1	

* And a eutectic at +1°. † And a eutectic at −4°.

Viscosity was measured in an all-glass, sealed, capillary viscometer[3] which was loaded as described elsewhere.[4] For the instrument used, the kinematic voscosity, ν (centistokes), was related to the efflux time, t (sec.), by the equation $\nu = 1{\cdot}8771 \times 10^{-2}t - 5{\cdot}44t^{-1}$. t varied between 50 and 68 sec., which is rather shorter than desirable, but experiments with water, which has a similar efflux time at room temperature, showed that the instrument was still behaving normally even though the second term in the above expression amounted to 10% of the first. However, the timing errors in individual runs were increased to about 0·2%. For

[2] Greenwood and Worrall, *J. Inorg. Nuclear Chem.*, in the press.
[3] Greenwood and Wade, *J. Appl. Chem.*, in the press.
[4] *Idem*, *J. Inorg. Nuclear Chem.*, in the press.

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this reason, the mean of six readings was taken at each temperature, the separate readings agreeing to 0·1 sec.

Density and surface tension were measured in the two-capillary dilatometer as already described.[4] The instrument was loaded *via* a double-bulb fractional recrystallisation unit.

Results.—The melting points in the system gallium trichloride–phosphorus oxychloride are summarised as a function of composition in Table 1. Fig. 2 shows that there is a maximum of 118·5° at the 1 : 1 ratio and eutectics at −1° (26·3 mole % of $POCl_3$) and −4° (89·5% of $POCl_3$). The compound $GaCl_3,POCl_3$ melts at 118·5° without decomposition and has a vapour pressure of <1 mm. at the m. p. (cf. $GaCl_3$, 63 mm.[5,6] and $POCl_3$, 1123 mm.[7] at 118·5°). The diagram also indicates a second compound, $GaCl_3,2POCl_3$, melting incongruently at about 77°,

TABLE 2. *Electrical conductivity of* $GaCl_3,POCl_3$ *between* 118° *and* 148°.

No.	t	$10^3\kappa$ (ohm^{-1} cm.$^{-1}$)	$\mu = \kappa V_M$ (cm.^{2} ohm^{-1})	$\mu\eta$ (cm.^{2} cP ohm^{-1})	No.	t	$10^3\kappa$ (ohm^{-1} cm.$^{-1}$)	$\mu = \kappa V_M$ (cm.^{2} ohm^{-1})	$\mu\eta$ (cm.^{2} cP ohm^{-1})
11	118·6°	1·263	0·2273	0·442	3	126·0°	1·390	0·2517	0·451
10	119·0	1·270	0·2286	0·442	19	126·6	1·402	0·2540	0·452
12	119·6	1·280	0·2305	0·443	1	127·0 *	1·408	0·2552	0·452
9	120·0	1·287	0·2319	0·444	2	127·0 †	1·406	0·2548	0·451
13	120·6	1·296	0·2337	0·444	20	127·0 ‡	1·408	0·2552	0·452
8	121·0	1·305	0·2354	0·445	21	127·6	1·420	0·2575	0·453
14	121·6	1·314	0·2370	0·446	22	128·0	1·427	0·2587	0·454
7	122·0	1·321	0·2384	0·446	30	130·6	1·474	0·2680	0·457
15	122·6	1·331	0·2405	0·447	23	133·0	1·521	0·2770	0·461
6	123·0	1·337	0·2414	0·447	29	135·6	1·574	0·2874	0·464
16	123·6	1·349	0·2437	0·448	24	138·0	1·617	0·2959	0·468
5	124·0	1·355	0·2449	0·449	28	140·6	1·672	0·3065	0·471
17	124·6	1·367	0·2471	0·449	25	143·0	1·718	0·3156	0·474
4	125·0	1·372	0·2482	0·450	27	145·6	1·766	0·3251	0·477
18	125·6	1·385	0·2505	0·451	26	148·0	1·827	0·3370	0·480

* + 0 hour; † + 2 hours; ‡ + 5 hours.

but this compound must be considered as less definite until further evidence for its existence is obtained from other property–composition diagrams.

The specific electrical conductivity, κ (ohm^{-1} cm.$^{-1}$) of the 1 : 1 compound between the m. p. and 148° is given in Table 2 which also lists the molar conductivity, $\mu = M\kappa/d = \kappa V_M$, and the molar conductivity reduced to unit viscosity, $\mu\eta$. Molten gallium trichloride–phosphorus oxychloride is seen to be a moderately good conductor : at the m. p. the specific conductivity is $1{\cdot}261 \times 10^{-3}$ ohm^{-1} cm.$^{-1}$ and this corresponds to a molar conductivity of 0·2270 cm.^{2} ohm^{-1} and a reduced conductivity of 0·442 cm.^{2} cP ohm^{-1}. In order to check that the drift in conductivity discussed in the experimental section had been eliminated, measurements were taken at 1° intervals between 127° and 119° (● on Fig. 3) and then at 1° intervals between 118·6° and 127·6° with a check reading at 127·0° (○ on Fig. 3). The run was then extended to 148° in 5° intervals (○), followed by a downward run (▲) in 5° intervals from 145·6°. It is clear that the results are reproducible even after the complex has been heated 30° above its m. p. The plot of log κ against $1/T°$ (K) which is shown in Fig. 3 is straight over the entire range, and corresponds to an activation energy E_κ of $4{\cdot}09_5$ kcal. mole^{-1}.

A D.C. current–voltage experiment carried out at 127° indicated two discontinuities corresponding to decomposition potentials of 1·10 and 1·58 v.

At currents greater than about 4 mA there was some blackening of the cathode surface which tended to increase the electrical capacity of the cell but there were no gaseous products of electrolysis. In a separate series of experiments an approximate value of the back-e.m.f. was obtained by electrolysing the molten compound for 1 min. at 5 mA and then measuring the cell voltage directly. In these conditions the electrolysis products rapidly diffused away from the electrodes and the voltmeter also drew current from the cell so that the observed e.m.f. fell rapidly with time. In a typical experiment the back-e.m.f. of about 1·0 v dropped to 0·9 v in 6 sec. after the cessation of electrolysis, to 0·5 v in 10 sec., and to 0·33 v in 60 sec.

[5] Laubengayer and Schirmer, *J. Amer. Chem. Soc.*, 1940, **62**, 1578.
[6] Fischer and Jübermann, *Z. anorg. Chem.*, 1936, **227**, 227.
[7] Arii, *Sci. Reports Tôhoku Imp. Univ.*, Ser. I., 1933, **22**, 182; *Chem. Abs.*, 1933, **27**, 3865.

FIG. 2. *Phase diagram of the system gallium trichloride–phosphorus oxychloride.*

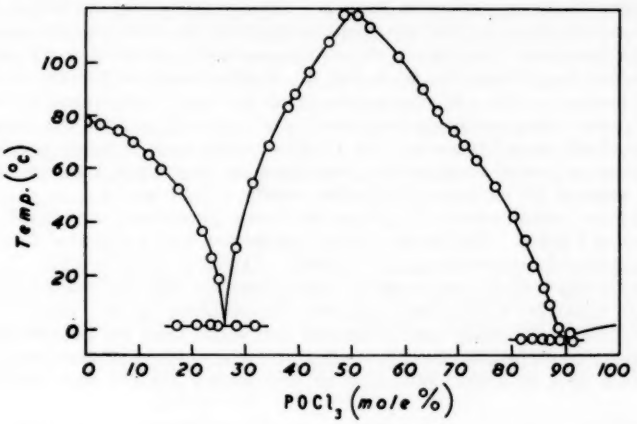
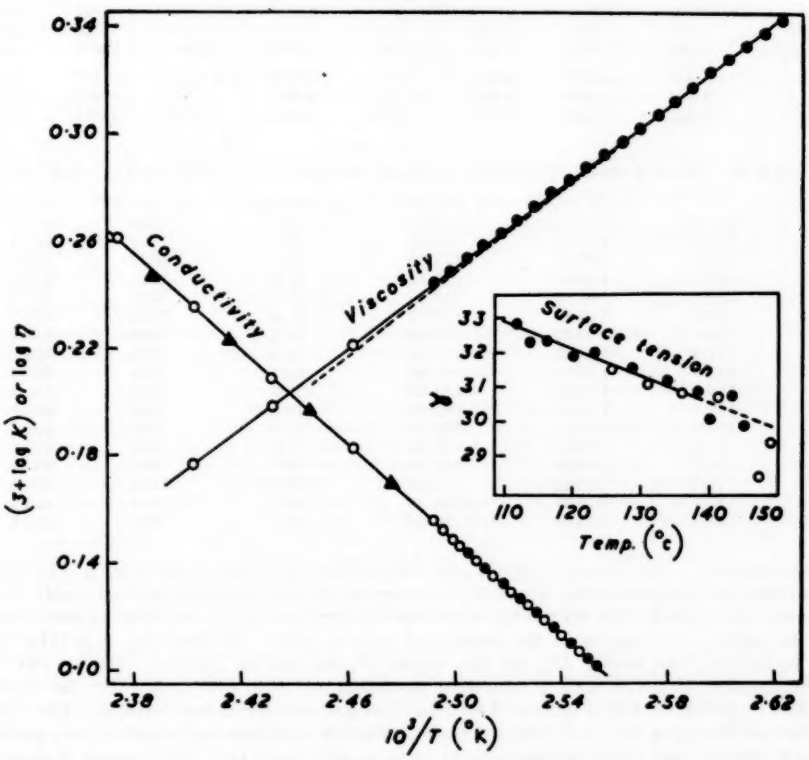


FIG. 3. *Conductivity, viscosity, and surface tension of the system gallium trichloride–phosphorus oxychloride.*



This suggests that the decomposition potential, measured as 1·10 v, is not seriously influenced by overvoltage and so may be taken as an indication of the free energy change of the cell reaction.

The viscosity results are set out in Table 3. Measurements were started at 128° and then taken at 1° intervals down to 108° at which temperature the complex had supercooled more than 10°. The kinematic viscosities (ν cs) so obtained were converted to dynamic viscosities (η cp) and plotted logarithmically (●) in Fig. 3. Further results at 5° intervals between 128° and 143° are plotted as (○). It appears that there is a small, discontinuous change in slope at about 117° : the activation energy increases by 4·5% from $E_\eta = 3{\cdot}41_4$ kcal. mole^{-1} above the m. p. to $3{\cdot}56_7$ kcal. mole^{-1} below it. At 118·5° the kinematic viscosity is 1·064 cs, almost exactly the same as that of water at 18°; the dynamic viscosity is 1·947 cp which is nearly twice that of water at 18° because of the higher density of the complex.

The density and molar volume of gallium trichloride–phosphorus oxychloride from 111° to 149° are shown in Table 4. The density can be represented with a standard deviation of 1·6 in the last decimal place by the equation $d_4^t = 1{\cdot}8281 - [1{\cdot}526 \times 10^{-3}(t - 120)]$.

The surface tension, which was measured simultaneously with the density, was less precise as the capillary diameters were rather larger than the optimum values : narrower tubes would increase the difficulty of loading the dilatometer and would limit the temperature range over which the density could be conveniently studied in a reasonably sized thermostat. Nevertheless, the results give a useful indication of the surface tension and related properties

TABLE 3. *Viscosity of molten and supercooled* $GaCl_3$,$POCl_3$ *between* 108° *and* 143°.

t	108·0°	109·0°	110·0°	111·0°	112·0°	113·0°	114·0°	115·0°
ν (cs)	1·194	1·180	1·167	1·154	1·142	1·128	1·115	1·104
η (cp)	2·205	2·178	2·152	2·125	2·102	2·075	2·049	2·027
t	116·0°	117·0°	118·0°	119·0°	120·0°	121·0°	122·0°	123·0°
ν (cs)	1·092	1·080	1·069	1·058	1·047	1·037	1·026	1·015
η (cp)	2·003	1·979	1·958	1·936	1·914	1·894	1·872	1·852
t	124·0°	125·0°	126·0°	127·0°	128·0°	133·0°	138·0°	143·0°
ν (cs)	1·005	0·994	0·985	0·975	0·965	0·921	0·878	0·838
η (cp)	1·831	1·809	1·791	1·711	1·753	1·666	1·581	1·503

TABLE 4. *Density and surface tension of molten* $GaCl_3$,$POCl_3$ *between* 111° *and* 149°.

No.	*t*	d_4^t (g. ml.$^{-1}$)	V_M (ml. mole^{-1})	γ (dyne cm.$^{-1}$)	$\omega = \gamma V_M^{2/3}$	[*P*]
17	111·6°	1·8410	178·95	32·7	1040	428·0
16	113·8	1·8374	179·29	32·3	1027	427·4
15	117·0	1·8323	179·79	32·3	1029	428·6
14	120·0	1·8281	180·21	31·8	1015	428·0
13	123·1	1·8233	180·68	32·0	1022	429·6
1	125·9	1·8192	181·09	31·6	1010	429·1
12	128·7	1·8148	181·53	31·5	1009	429·9
2	131·1	1·8112	181·89	31·1	998	429·5
11	133·7	1·8071	182·30	31·1	999	430·4
3	136·1	1·8037	182·64	30·8	990	430·1
10	138·1	1·8005	182·97	30·8	991	430·9
9	140·0	1·7975	183·27	30·0	967	428·8
4	141·4	1·7956	183·47	30·6	989	431·6
8	143·1	1·7930	183·73	30·7	992	432·4
7	145·0	1·7903	184·01	29·8	963	429·8
5	147·1	1·7869	184·36	28·3	917	425·3
6	149·0	1·7840	184·66	29·3	950	429·6

of the complex. The values obtained are summarised in Table 4 and Fig. 3. In calculating these values, a meniscus correction appropriate to capillaries of approximately 1 mm. diameter was applied; this relates the observed capillary rise, h_0, to the true capillary rise, h, and the radius, r, by means of the equation $h = h_0 + (r/3) - (0{\cdot}1288r^2/h_0) + (0{\cdot}1312r^3/h_0^2)$. The correction was about 2% of the value of the surface tension. Below 140° the surface tension is given with a standard deviation of 0·13 dyne cm.$^{-1}$ by the relation $\gamma = 32{\cdot}0 - 0{\cdot}076(t - 120)$. Above 140° the results are somewhat erratic. The molar surface free energy ω (erg mole$^{-2/3}$), calculated from the experimental points, is also listed in Table 4; below 140° it can be represented by $\omega = 1022 - 1{\cdot}81(t - 120)$, where 1·81 is the Eötvös constant k. A very approximate idea of the critical temperature may be obtained

from this expression on the assumption that the linear relation holds until the molar surface free energy becomes zero. This leads to a critical temperature of 685° and a boiling point of approximately 365° if the b. p. is taken as 2/3 of the critical temperature on the absolute scale.

The parachor values ($[P] = V_M\gamma^{\frac{1}{4}}$) calculated from the molar volume and surface tension are also listed in Table 4. As the vapour pressure of the complex is only of the order of 1 mm. at these temperatures the neglect of the gas density has negligible effect on the calculation. Between 111° and 140° the parachor has a mean value of 429·2 with a standard deviation of ±1·1. The six readings above 140° give a mean value of 429·6 but with a standard deviation of 2·5. The average of all values is 429·3 ± 1·6. The value calculated by McGowan's method,[8] by use of the predicted value of 99·0 for the parachor of gallium, is 428·7 in excellent agreement with the observed value.

Discussion

Gallium trichloride and phosphorus oxychloride form a 1 : 1 addition compound which melts at 118·5° to give a stable, colourless liquid. Its properties in the molten state at 118·5° are summarised in Table 5 which also lists the corresponding properties of the

Table 5. *Comparison of the properties of* Ga_2Cl_6, $GaCl_3$,$POCl_3$, *and* $POCl_3$ *at their respective m. p.s.*

Property	Ga_2Cl_6 [a]	$GaCl_3$,$POCl_3$	$POCl_3$
Mol. wt.	2 × 176·09	329·44	153·35
M. p.	77·75°	118·5°	1°
B. p.	200°	est. 365°	105°
p (mm. Hg)	10·4 [j] (63) [j]	<1	11·0 [k] (1123) [k]
d (g. ml.$^{-1}$)	2·0536 (1·9685)	1·8304	1·7104 [b] (1·4930) [b]
Temp. coef. of d	2·09 × 10^{-3}	1·526 × 10^{-3}	1·85 × 10^{-3}
V_M (ml. mole^{-1})	2 × 85·72 (89·45)	179·98	89·66 [b] (102·71) [b]
ν (cs)	0·8877 (0·539)	1·064	0·866 [c] (0·36) [d]
η (cp)	1·823 (1·061)	1·947	1·465 [c] (0·53) [d]
E_η (kcal. mole^{-1})	$3{\cdot}63_6$	$3{\cdot}41_4$	~1·90 [c]
ϕ (cp^{-1})	0·5486 (0·943)	0·5137	0·683 [c] (1·89) [d]
B (ml. cp g.$^{-1}$)	5·75 × 10^{-2}	7·89 × 10^{-2}	6·45 × 10^{-2} [f]
γ (dyne cm.$^{-1}$)	27·3 (23·1)	32·1	34·5 [g] (20·1) [g]
Temp. coef. of γ	0·105	0·076	0·122 [g]
ω (erg mole$^{-2/3}$)	842·5 (732·4)	1025	686·6 [g] (440·8) [g]
k (Eötvös)	2·70	1·81	2·20 [g]
$[P]$	395·5 (calc. 418·0)	429·2 (calc. 428·7)	217·6 [g] (calc. 219·7)
κ (ohm^{-1} cm.$^{-1}$)	1·86 × 10^{-6} [h] (2·0 × 10^{-6})	1·261 × 10^{-3}	1·25 × 10^{-6} [i] (2·3 × 10^{-6}) [i]
E_κ (kcal. mole^{-1})	—	$4{\cdot}09_5$	—
μ (cm.^{2} ohm^{-1})	1·6 × 10^{-4} (1·8 × 10^{-4})	0·2270	1·13 × 10^{-4} [i] (2·2 × 10^{-4}) [i]
$\mu\eta$ (cm.^{2} cp ohm^{-1})	2·9 × 10^{-4} (1·9 × 10^{-4})	0·442	1·6 × 10^{-4} [i] (1·2 × 10^{-4}) [i]

[a] Taken or calc. from data in ref. 4. [b] Values from Bowden and Morgan (*Phil. Mag.*, 1940, **29**, 367) which are concordant with those of Ramsay and Shields (*J.*, 1893, **63**, 1089) and Sugden, Reed, and Wilkins (*J.*, 1925, 1525) but disagree with more recent results of Gutmann (*Monatsh.*, 1952, **83**, 164) which are apparently in error by *ca.* 1%. [c] Gutmann (*loc. cit.*) and Lutschinsky (*Z. anorg. Chem.*, 1935, **223**, 210); Bowden and Morgan (*loc. cit.*) give $\nu = 0{\cdot}883$ cs, $\eta = 1{\cdot}510$ cp, and $\phi = 0{\cdot}662$ cp^{-1} at 1°. [d] By logarithmic extrapolation of data by Gutmann (*loc. cit.*). [e] Data by Bowden and Morgan (*loc. cit.*) give a linear plot of slope 1·92 kcal. mole^{-1}. Activation energies calculated from data by Gutmann and Lutschinsky (*locc. cit.*) decrease from 2·09 and 2·16 kcal. mole^{-1} respectively near the m. p. to 1·68 and 1·62 at higher temps. [f] Calc. from Gutmann (*loc. cit.*) below 25°; the plot of specific volume against fluidity curves slightly. Lutschinsky (*loc. cit.*) gives $B = 7{\cdot}12 \times 10^{-2}$ ml. cp g.$^{-1}$. [g] Extrapolated from data by Sugden, Reed, and Wilkins (*loc. cit.*): Ramsay and Shields (*loc. cit.*) imply values of $\gamma = 34{\cdot}1$ and 19·3 dyne cm.$^{-1}$ at 1° and 118·5° with a temp. coefficient of γ of 0·126 dyne cm.$^{-1}$ deg.$^{-1}$; $\omega = 683{\cdot}8$ at 1° and 434·2 at 118·5°; Eötvös constant $k = 2{\cdot}12_5$. [h] Ref. 2. [i] Extrapolated from data by Gutmann (*loc. cit.*). Other values are $\kappa_{25} = 1{\cdot}7 \times 10^{-6}$ (Walden, *Z. phys. Chem.*, 1903, **43**, 445) and 1 × 10^{-6} ohm^{-1} cm.$^{-1}$ (Payne, *J.*, 1953, 1052). [j] Refs. 5 and 6. [k] Ref. 7 and Lutschinsky and Likhacheva, *J. Phys. Chem. U.S.S.R.*, 1937, **9**, 65.

donor and acceptor moieties at their respective m. p.s. A further comparison of the three compounds all at 118·5° is also given, the values for gallium trichloride and phosphorus oxychloride being recorded in parentheses after the figures referring to data at the m. p. It is seen that complex formation is accompanied by an appreciable increase in the m. p. and b. p. of the system, the values for the complex being above those of both

[8] McGowan, *Chem. and Ind.*, 1952, 495.

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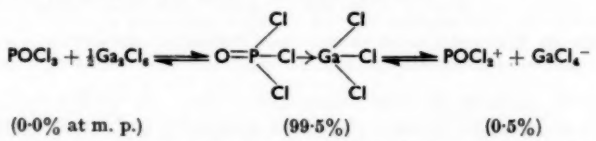
components. The kinematic and dynamic viscosities of the complex are also greater than the values for either component at their respective m. p.s and this effect is enhanced if all three compounds are compared at 118·5°; for example, the dynamic viscosity of the complex is twice that of gallium trichloride and nearly four times that of phosphorus oxychloride. Properties depending directly or indirectly on molar volume also increase on complex formation. These properties, which include the molar volume itself, V_M, Batschinski's constant B, the molar surface free energy ω, and the parachor $[P]$ will be discussed more fully later.

Perhaps the most noticeable change during complex formation is the 1000-fold increase in electrical conductivity. This implies a great increase in the number of free ions and, as the activation energies of viscosity (E_η) and conduction (E_κ) are about the same, it is possible to use the reduced conductivity ($\mu\eta$) in these units to indicate the percentage degree of ionic dissociation.[9] The figures in Table 5 therefore suggest that, whereas the degree of ionic dissociation of molten gallium trichloride and liquid phosphorus oxychloride are both of the order of 10^{-4}%, yet the corresponding value for the 1 : 1 complex is about ½%. The calculation should be correct to within a factor of 2 or 3. It is perhaps unnecessary to stress that conduction in the molten complex is not due to impurities, since the conductivity only appears when the two vacuum-distilled, non-conducting components are mixed, and its magnitude would require a concentration of several grams per litre of some fully ionised impurity such as potassium chloride. The degree of ionic dissociation of molten gallium trichloride–phosphorus oxychloride may be compared with the values obtained for certain co-ordination compounds of boron trifluoride:[9] the value of ½% is greater than the degree of dissociation of ester and ether complexes, about the same as that of boron trifluoride–triethylamine, and somewhat less than the values obtained for the alcohol complexes and hydrates. A rough comparison is also possible with molten gallium trichloride–benzoyl chloride [1] and molten stannic chloride–di(phosphorus oxychloride).[10] Thus, if one assumes that the density and viscosity of gallium trichloride–benzoyl chloride and gallium trichloride–phosphorus oxychloride are approximately the same, then the reduced conductivity of the benzoyl chloride complex, and hence its degree of ionic dissociation, is 0·3—0·4% which is very close to the value obtained for gallium trichloride–phosphorus oxychloride. The complex of stannic chloride with phosphorus oxychloride, however, seems to have a degree of dissociation which is less by a power of ten, as the published values of the specific conductivity and density imply a molar conductivity of $2{\cdot}5 \times 10^{-2}$ cm.^{2} ohm^{-1} and, if the viscosity is again taken as about 2 cP, then the reduced conductivity $\mu\eta$ is approximately 0·05. Only if the viscosity were as great as 15—20 cP would the estimated degree of ionic dissociation approach those of the gallium trichloride complexes discussed here.

The nature of the ionic species present in molten gallium trichloride–phosphorus oxychloride has not been established directly by the present investigation. There were no gaseous products of electrolysis. By analogy with the complex gallium trichloride–benzoyl chloride [1] the compound might be formulated as one in which a chlorine atom of phosphorus oxychloride was the electron donor, the compound so formed dissociating reversibly as dichloro-oxophosphonium tetrachlorogallate:



Such a scheme would be consistent with the transport measurements made on solutions of the related compound aluminium trichloride–phosphorus oxychloride which indicate

[9] Greenwood and Martin, *J.*, 1953, 1427.
[10] Garner and Sugden, *J.*, 1929, 1298.

dissociation as $POCl_2^+AlCl_4^-$.[11] A test for this structure in the molten state might be obtained from chlorine-isotope exchange, but the more direct approach which is being followed is the investigation of the Raman spectrum of the solid and the melt. Similar experiments on saturated solutions of antimony pentachloride in phosphorus oxychloride have already been taken to indicate the presence of the ions $POCl_2^+$ and $SbCl_6^-$.[12] The alternative formulation of phosphorus oxychloride complexes in terms of electron donation by the oxygen atom, rather than by a chlorine atom,[10,13] is considered less satisfactory in view of the above arguments. Indirect evidence for the chlorine-donating structures is also afforded by the fact that, whereas phosphorus oxychloride forms an unstable addition compound with boron trichloride, it does not donate at all to the stronger electron-acceptor boron trifluoride.[14] This is difficult to interpret if oxygen is the donor atom, but is understandable if chlorine is the electron donor since the BCl_4 unit, though unstable, is nevertheless more stable than the unsymmetrical BF_3Cl unit.[1]

The foregoing discussion has shown that, although gallium trichloride–phosphorus oxychloride is dissociated into ions to the extent of about $\frac{1}{2}\%$, the bulk of the molten phase comprises undissociated molecules or ion-pairs. It is therefore of interest to consider the volume change which occurs during complex formation. If two compounds in a condensed phase react to give an addition compound, one would expect a contraction in volume as a covalent, donor-acceptor bond between each pair of molecules is replacing the weaker van der Waals attraction : $D + A \longrightarrow D{:}A$. This contraction might be expected to be approximately the same for different systems and it is known that for complexes of boron trifluoride and for other donor-acceptor systems the decrease in molar volume is frequently about 10 ml.[15] For gallium trichloride–phosphorus oxychloride a contraction of 12·2 ml. mole^{-1} is obtained on complex formation if this is measured at the m. p. of the complex (118·5°). The agreement with other donor–acceptor systems, however, may be fortuitous since, in this particular instance, the reaction is not one between monomeric donor and monomeric acceptor but one between monomeric donor and dimeric acceptor : $D + \frac{1}{2}A_2 \longrightarrow D{:}A$. The contraction might therefore be expected to be only half that observed for monomeric systems as only the ligand molecules become involved in extra bonding. Indeed, as the dimeric acceptor molecules have a bridge structure, two co-ordinate bonds are broken for each two formed, so that one might even imagine the reaction to occur with no change in volume. In fact, the volume change observed will depend on the temperature of comparison because the coefficients of expansion of the components and the complex are not the same. For example, if the comparison of molar volumes is carried out arbitrarily at the respective m. p.s of the various compounds, then Table 5 shows that complex formation involves an expansion of 4·6 ml. mole^{-1} rather than a contraction.

Perhaps more significant is the change in value of Batschinski's constant B which is obtained from the slope of the graph of specific volume against fluidity : $v = B\phi + b$ where b is a constant. Batschinski's constant is related to the size of the flow units in the liquid so that the figures in Table 5 imply an increase in size of these kinetic units on complex formation. Rather different results would have been expected had the degree of ionic dissociation been considerably larger. The plot of specific volume against fluidity is also relevant to a discussion of the discontinuities which occur in the physical properties of supercooled liquids.[16] The present fluidity data for gallium trichloride–phosphorus oxychloride both above and below the m. p. can be represented by a single, slightly curved line, so that the small discontinuity observed in the Arrhenius plot of viscosity (Fig. 3) must be considered indecisive for this compound.

[11] Gutmann and Himml, *Z. phys. Chem.* (*Frankfurt*), 1955, **4**, 157.
[12] Maschka, Gutmann, and Sponer, *Monatsh.*, 1955, **86**, 52.
[13] Groeneveld, Proc. Symp. Co-ord. Chem., Copenhagen, 1953, 140; Payne, *ibid.*, p. 146.
[14] Burg and Ross, *J. Amer. Chem. Soc.*, 1943, **65**, 1637.
[15] Greenwood and Martin, *J.*, 1953, 4132.
[16] *Idem, Proc. Roy. Soc.*, 1952, *A*, **215**, 46.

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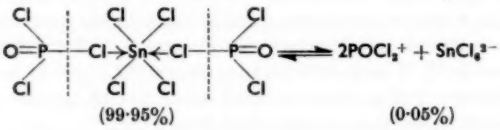
The possible existence of the incongruently melting 2 : 1 compound gallium trichloride–di(phosphorus oxychloride) calls for brief comment. Such compounds of phosphorus oxychloride are well known but all may not have the same structure. Thus stannic chloride–di(phosphorus oxychloride) has been formulated as $(POCl_2^+)_2\ SnCl_6^{2-}$,[17] and even though the calculation presented above indicates that the degree of ionic dissociation is only of the order of 0·05%, the undissociated form can still be written in a way which implies electron donation from two chlorine atoms towards the central tin atom :



On the other hand gallium trichloride–di(phosphorus oxychloride) might merely be a solvate in which the second phosphorus oxychloride molecule is attached to the phosphorus atom rather than to the gallium :

$$POCl_2,POCl_2,Cl\rightarrow GaCl_3 \rightleftharpoons POCl_2,POCl_2^+ + GaCl_4^-$$

The alternative formulation involving five co-ordinate gallium seems less probable. A similar difficulty arises in the system of phosphorus oxychloride with titanium tetrachloride where two congruently melting compounds, $TiCl_4,POCl_3$ and $TiCl_4,2POCl_3$ have finally been established.[18] In other systems, such as those with zirconium and hafnium tetrachlorides, even the formulæ of the complexes formed are undecided and mole ratios $POCl_3 : MCl_4$ of 2 : 1, 1 : 1, 1 : 2, and 2 : 3 have been suggested.[19] It may well be that some of the supposed compounds are azeotropes rather than chemical individuals but there is clearly a need both for phase studies to establish the formulæ of the addition compounds and for electrochemical investigation to establish the degree of ionic dissociation of the complexes. Raman spectra or *X*-ray data could then be used to elucidate the structure of the groups so formed by deciding which atoms were involved in the donor–acceptor bonding.

[*Added, February* 11*th*, 1957.—The conductivity of $TiCl_4,2POCl_3$ at its m. p., 105°, has been reported as $1{\cdot}38 \times 10^{-3}$ ohm^{-1} cm.$^{-1}$;[20] this corresponds to a molar conductivity of 0·384 ohm^{-1} cm.$^{-1}$ and a reduced conductivity of about 0·75 if the viscosity is assumed to be 2 cP. The implied degree of ionisation, ¾%, is similar to that found for $GaCl_3,POCl$ but considerably larger than that of $SnCl_4,2POCl_3$. A phase study[21] of the system $ZrCl_4$–$POCl_3$ indicates two congruently melting compounds $ZrCl_4,POCl_3$, m. p. 205°, and $ZrCl_4,2POCl_3$, m. p. 184·7°, and this agrees well with cryoscopic results in nitrobenzene.[22] However, distillation gives a product which can be represented approximately as $3ZrCl_4,2POCl_3$.[23]]

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The University, Nottingham. [*Received, September* 6*th*, 1956.]

[17] Gutmann, *Z. anorg. Chem.*, 1952, **270**, 179.
[18] Groeneveld, van Spronsen, and Kouwenhoven, *Rec. Trav. chim.*, 1953, **72**, 950.
[19] van Arkel and de Boer, *Z. anorg. Chem.*, 1924, **141**, 289; Gruen and Katz, *J. Amer. Chem. Soc.*, 1949, **71**, 3843; Larsen, Howatson, Gammill, and Wittenberg, *ibid.*, 1952, **74**, 3489.
[20] Payne, *Rec. Trav. chim.*, 1956, **75**, 620.
[21] Sheka and Voitovich, *Zhur. neorg. Khim.*, 1956, **1**, 964.
[22] Larsen and Wittenberg, *J. Amer. Chem. Soc.*, 1955, **77**, 5850.
[23] Nisel'son and Ivanov-Emin, *Zhur. neorg. Khim.*, 1956, **1**, 1766.

292. *Intermediates and Dyes. Part V.* Derivatives of Thiophanthrene-4 : 9-quinone.*

By Arnold T. Peters and Derek Walker.

Derivatives of thiophanthrene-4 : 9-quinone and of β-thiophanthrene-4 : 9-quinone have been examined, with special reference to those compounds with easily replaceable chlorine atoms.

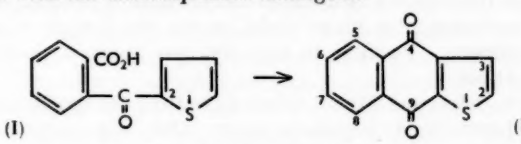
3 : 6-Dichloro-2-2′-thenoylbenzoic acid, best prepared from 3 : 6-dichlorophthalic anhydride by the Grignard reaction, gave the yellow 5 : 8-dichlorothiophanthrene-4 : 9-quinone, converted into 8-chloro-5-amino- and 5 : 8-diamino-thiophanthrene-4 : 9-quinone, which dye cellulose acetate rayon and Nylon bluish-red and bluish-violet shades, respectively, bluer than the shades given by the anthraquinone analogues.

3 : 6-Dichloro-2-(2 : 5-dimethyl-3-thenoyl)benzoic acid was prepared by the Friedel–Crafts reaction, and was cyclised to the yellow 5 : 8-dichloro-1 : 3-dimethyl-β-thiophanthrene-4 : 9-quinone, converted into dyes which are redder than the anthraquinone analogues.

Friedel–Crafts reactions between 3 : 6-dichlorophthalic anhydride and 2- or 3-methylthiophen were also examined; in the latter case, it was established by synthesis that the initial product was 3 : 6-dichloro-2-(3-methyl-2-thenoyl)benzoic acid, with only 5% of the 4-methyl isomer.

Compared with the anthraquinone analogues, there is loss of tinctorial power when a benzene ring is replaced by a thiophen ring.

In Part IV,* intermediates and dyes based on benzothiophanthrene-6 : 11-quinone (6 : 11-dihydro-6 : 11-dioxobenzo[*b*]thiophanthrene) were investigated. The present work includes an examination of similar derivatives from thiophanthrene-4 : 9-quinone (II), and a comparison with the anthraquinone analogues.



(I) (II)

The parent compound (II) was obtained by cyclisation of 2-2′-thenoylbenzoic acid (I), which we prepared from phthalic anhydride and thiophen by the Friedel–Crafts reaction, in spite of conflicting claims in the literature. It appears that polymerisation of thiophen predominates at low temperatures. According to Etienne,[2] the carboxylic acid (I) was obtained in 80% yield from 2-thienylmagnesium iodide.

For preparation of 5 : 8-disubstituted derivatives of the quinone (II), containing easily replaceable groups, the use of thiophen-2 : 3-dicarboxylic acid anhydride as intermediate was impracticable owing to the very low yields obtained by oxidising 2-acetyl-3-methylthiophen (cf. other workers [3]).

On applying the above successful Friedel–Crafts reaction for the acid (I) to the interaction of 3 : 6-dichlorophthalic anhydride and thiophen, we obtained only 4% of 3 : 6-dichloro-2-2′-thenoylbenzoic acid, but Lee and Weinmayr's method [4] afforded an 81·4% yield. Cyclisation to the bright yellow 5 : 8-dichlorothiophanthrene-4 : 9-quinone was best (21·5%) achieved by aluminium chloride in nitrobenzene. To determine the conditions for replacing the chloro-groups in this compound, experiments were carried out with 1 : 4-dichloroanthraquinone. Attempts with methylamine under a variety of conditions gave only poor yields of the 1 : 4-bismethylamino- or 1-chloro-4-methylamino-compound, but fusion with *N*-methyltoluene-*p*-sulphonamide in presence of sodium acetate and copper acetate, followed by hydrolysis, afforded 30% of the monocondensation

* Part IV, *J.*, 1956, 1429.

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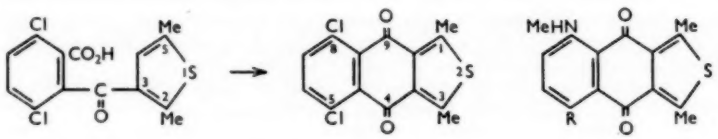
product (cf. Ullmann and Bielig [5]). 5 : 8-Dichlorothiophanthrene-4 : 9-quinone similarly yielded 44% of 5 : 8-ditoluene-*p*-sulphonamido- and 40·5% of 8-chloro-5-toluene-*p*-sulphonamido-thiophanthrene-4 : 9-quinone, longer reaction giving 89% of the ditoluene-*p*-sulphonamide. Almost quantitative hydrolysis of the two sulphonamides by 95% sulphuric acid at room temperature afforded the free amines.

The orientation of the amino-chloro-derivative was proved by synthesis of the isomeric 8-amino-5-chloro-analogue. 3-Nitrophthalic anhydride and 2-thienylmagnesium bromide yielded 3- and 6-nitro-2-2′-thenoylbenzoic acid; cyclisation of both of these acids (with rearrangement of the 3-nitro-compound) yielded solely 5-nitrothiophanthrene-4 : 9-quinone (Weinmayr and Schroeder [1]). However, reduction of 3-nitro-2-2′-thenoylbenzoic acid by Mitter's method [6] gave 96% of the corresponding amine. Cyclisation by 95% sulphuric acid at 135—140° yielded 8-aminothiophanthrene-4 : 9-quinone, converted into the 8-benzamido-derivative. Subsequent chlorination gave 60% of 8-benzamido-5-chlorothiophanthrene-4 : 9-quinone, hydrolysed by sulphuric acid to 8-amino-5-chlorothiophanthrene-4 : 9-quinone. Unfortunately, when 6-nitro-2-2′-thenoylbenzoic acid was treated as described, the resulting 5-benzamidothiophanthrene-4 : 9-quinone could not be chlorinated satisfactorily.



(III) (IV) (V)

5-Amino-8-chlorothiophanthrene-4 : 9-quinone dyes cellulose acetate rayon and Nylon red shades, bluer than those shown by 4-amino-1-chloroanthraquinone; and 5 : 8-diaminothiophanthrene-4 : 9-quinone gives bluish-violet shades, much bluer than those given by 1 : 4-diaminoanthraquinone. Fastness to light and gas fumes is similar to that of the anthraquinone derivatives.

It was of interest to determine if the position of the thiophen ring affected the properties of dyes in the thiophanthrene-4 : 9-quinone series. Only one compound containing the β-thiophanthrene-4 : 9-quinone (naphtho[2,3-*c*]thiophen-4 : 9-quinone) structure has been described, *viz.*, 1 : 3-dimethyl-β-thiophanthrene-4 : 9-quinone.[7] We prepared 2 : 5-dimethylthiophen from acetonylacetone by a modification of Paal's method.[8] Although the Friedel–Crafts reaction proved unsuitable for preparing 3 : 6-dichloro-2-2′-thenoylbenzoic acid, derivatives from methylthiophens could be prepared by this method : *e.g.*, 2 : 5-dimethylthiophen and 3 : 6-dichlorophthalic anhydride, best at 40—60°, gave the carboxylic acid (III), which with aluminium chloride in nitrobenzene at 130—140° gave 42·4% of the yellow 5 : 8-dichloro-1 : 3-dimethyl-β-thiophanthrene-4 : 9-quinone (IV). Other methods of cyclisation gave lower yields.

On attempting to replace the chlorine atoms of the quinone by the toluene-*p*-sulphonamido-group, decomposition occurred. However, whereas alcoholic methylamine failed

[1] Ernst, *Ber.*, 1886, **19**, 3278; Steinkopf and Butkiewicz, *Annalen*, 1914, **407**, 94; Buu-Hoï, Hoán, and Xuong, *Rec. Trav. chim.*, 1950, **69**, 1083; Lee and Weinmayr, U.S.P. 2,497,334/1950; Weinmayr and Schroeder, *J., Amer. Chem. Soc.*, 1952, **74**, 4353.

[2] Etienne, *Bull. Soc. chim. France*, 1947, 634.

[3] Demuth, *Ber.*, 1885, **18**, 3024; Gerlach, *Annalen*, 1892, **267**, 155; Linstead, Noble, and Wright, *J.*, 1937, 917.

[4] Lee and Weinmayr, U.S.P. 2,513,572—4/1950.

[5] Ullmann and Bielig, *Annalen*, 1911, **381**, 11.

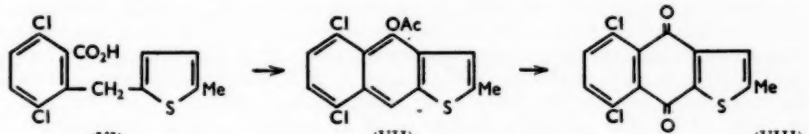
[6] Mitter, *J. Indian Chem. Soc.*, 1930, **7**, 625.

[7] Steinkopf, Barlag, and von Petersdorff, *Annalen*, 1939, **540**, 7; Goncalves and Brown, *J. Org. Chem.*, 1952, **17**, 698.

[8] Paal, *Ber.*, 1885, **18**, 2252.

to give dyes from 5 : 8-dichlorothiophanthrene-4 : 9-quinone, it gave with the 1 : 3-dimethyl-quinone (IV), in presence of pyridine and copper acetate at 135—140°, moderate yields of the 5-chloro-8-methylamino- (V; R = Cl) and 5 : 8-bismethylamino-derivative (V; R = NHMe). Refluxing the quinone (IV) in aniline with a trace of copper acetate gave the maroon 5-anilino-8-chloro-1 : 3-dimethyl-β-thiophanthrene-4 : 9-quinone. The dyes of the β-thiophanthrene-4 : 9-quinone series do not form alkaline dithionite (hydrosulphite) vats, unlike the thiophanthrene-4 : 9-quinones. The quinone (V; R = NHMe) dyed cellulose acetate rayon and Nylon violet, compared with the much bluer shades shown by 1 : 4-bismethylaminoanthraquinone; also redder than the anthraquinone analogues were the chloro-derivative (V; R = Cl) and the above anilino-compound, which gave orange and salmon-pink shades, respectively. This hypsochromic effect is in contrast to the bathochromic shift given by derivatives of the normal thiophanthrene-4 : 9-quinones. Replacement of one benzene ring by a thiophen ring in such anthraquinoid dyes, however, leads to loss of colour value.

Slow addition of 2-methylthiophen to 3 : 6-dichlorophthalic anhydride in nitrobenzene at 40—45° gave 57% of 3 : 6-dichloro-2-(5-methyl-2-thenoyl)benzoic acid; direct cyclisation of this proved unsuccessful; prior reduction by zinc dust and aqueous ammonia gave the corresponding thenyl derivative (VI), which with zinc chloride in boiling acetic



(VI) (VII) (VIII)

anhydride and acetic acid afforded an almost quantitative yield of 4-acetoxy-5 : 8-dichloro-2-methylthiophanthrene (VII), oxidised by potassium dichromate in acetic acid in 82% yield to 5 : 8-dichloro-2-methylthiophanthrene-4 : 9-quinone (VIII). Attempted replacement of chlorine therein by amino, methylamino, or toluene-*p*-sulphonamido, gave only traces of the required products, but refluxing with aniline and copper acetate yielded 36% of the intense greenish-blue dye, 5 : 8-dianilino-2-methylthiophanthrene-4 : 9-quinone.

The conditions favourable for condensation of 2-methylthiophen and 3 : 6-dichlorophthalic anhydride were applied to 3-methylthiophen, and gave unexpectedly 3 : 6-dichloro-2-(3-methyl-2-thenoyl)benzoic acid (IX) and only a small amount of the 4'-methyl isomeride. Heating the acid (IX) with aluminium chloride and sodium chloride at 130—135° gave only 2% of the yellow 5 : 8-dichloro-3-methylthiophanthrene-4 : 9-quinone (X). The acid (IX) was reduced with zinc dust and aqueous ammonia to the thenylbenzoic

(IX) (X)

acid, which with boiling acetic anhydride, acetic acid, and zinc chloride gave a colourless product slowly soluble in aqueous sodium hydrogen carbonate and unchanged by boiling aqueous sodium hydroxide; such properties indicated that cyclisation had not occurred and that the anhydride of the carboxylic acid had not been formed, and it is considered that the colourless derivative is 2-(5-acetyl-3-methyl-2-thenyl)-3 : 6-dichlorobenzoic acid. The constitution of the carboxylic acid (IX) was confirmed by synthesis.

2-Chloromercuri-3-methylthiophen, obtained by Volhard's method,[9] was converted

[9] Volhard, *Annalen*, 1897, **267**, 180.

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into 2-iodo-3-methylthiophen,[10] the Grignard reagent from which with 3 : 6-dichlorophthalic anhydride gave the acid (XI).

The Friedel–Crafts reaction above with 3-methylthiophen gave, as by-product, probably 5% of 3 : 6-dichloro-2-(4-methyl-2-thenoyl)benzoic acid, as indicated by the formation of 2% of the quinone (X) by cyclisation.

Experimental

2-2′-Thenoylbenzoic Acid.—Phthalic anhydride (29·6 g., 1 mol.), aluminium chloride (58·7 g., 2·2 mols.), and nitrobenzene (100 ml.) were stirred at 55—60° for 1 hr., then cooled to 40°, and thiophen (16·8 g., 1 mol.) was added dropwise during 2 hr. at 40—45°; after a further hr. at 40—45°, and then 1 hr. at 50—55° the mass was added to concentrated hydrochloric acid (13 ml.) in water (1100 ml.) and stirred vigorously for 1 hr. The nitrobenzene layer was separated, the solvent removed with steam, and the acid purified through its aqueous sodium carbonate solution. The acid crystallised from dilute acetic acid in colourless leaflets, m. p. 146—147° (26·8 g., 57·7%) (Found : C, 61·7; H, 3·2; S, 14·2. Calc. for $C_{12}H_8O_3S$: C, 62·1; H, 3·5; S, 13·8%).

3 : 6-Dichlorophthalic Anhydride.—This was separated from a mixture containing 3 : 4-, 4 : 5-, and 3 : 6-dichloro-derivatives through the calcium salt of the acid, by Villiger's method.[11]

3 : 6-Dichloro-2-2′-thenoylbenzoic Acid.—(*a*) 3 : 6-Dichlorophthalic anhydride (43·4 g., 1 mol.), replacing the phthalic anhydride in the above experiment, gave the carboxylic acid, purified by several precipitations from its aqueous sodium carbonate solution, and by crystallisation from dilute acetic acid in colourless, hexagonal plates, m. p. 146—147° (Found : C, 47·5; H, 1·9; Cl, 23·7; S, 10·8. Calc. for $C_{12}H_6O_3Cl_2S$: C, 47·8; H, 2·0; Cl, 23·6; S, 10·6%).

The *methyl ester*, prepared by the Fischer–Speier method, distilled at 180°/0·9 mm., and had m. p. 63—64° (Found : C, 49·9; H, 2·3; Cl, 22·3; S, 9·8. $C_{13}H_8O_3Cl_2S$ requires C, 49·5; H, 2·6; Cl, 22·5; S, 10·2%).

(*b*) In preparing the following Grignard reagent, and in the condensation, nitrogen was passed continuously. Magnesium turnings (1·5 g., 1·25 mols.), a crystal of iodine, dry ether (60 ml.), and a few drops of 2-bromothiophen were warmed until reaction began, and 2-bromothiophen (total wt., 8·2 g., 1 mol.) in ether (12 ml.) was added during 1 hr., under reflux; after refluxing further for 1 hr. and cooling to 20°, the mixture was run into a stirred solution of 3 : 6-dichlorophthalic anhydride (10·8 g., 1 mol.) in dry benzene (260 ml.) at 50°. The whole was refluxed for 1 hr., then cooled to 20°, water (85 ml.) added gradually, refluxing continued for 1 hr., the mixture cooled to 25°, magnesium oxide (1·7 g.) added, and the whole shaken for 3 hr. at 20—25°. The slightly alkaline aqueous layer was combined with aqueous extracts of the solvent layer, and acidification gave the carboxylic acid, which crystallised from benzene in pale yellow plates, m. p. 142° (12·25 g., 81·4%). This product, although not quite so pure as the sample as prepared above, was used for further experiments.

5 : 8-Dichlorothiophanthrene-4 : 9-quinone.—The acid chloride, prepared from the above carboxylic acid by thionyl chloride, was treated in carbon disulphide or nitrobenzene with aluminium chloride (2·2 mols.) at room temperature, but it gave only a trace of quinone; higher temperatures gave a similar result. The use of concentrated sulphuric acid at 165—170° for 5 min. gave 5·2% of quinone, and phosphoric oxide (3 mols.) in nitrobenzene at 130—140° for 30 hr. afforded 17·5%. The best method of cyclisation was to treat the carboxylic acid (4 g.) with aluminium chloride (8 g.) in nitrobenzene (60 ml.) for 24 hr. at room temperature; removal of solvent with steam gave the quinone, which sublimed *in vacuo* at 170° as bright yellow needles, m. p. 225—226° (Found : C, 51·0; H, 1·3; Cl, 24·8; S, 11·3. Calc. for $C_{12}H_4O_2Cl_2S$: C, 50·9; H, 1·4; Cl, 25·1; S, 11·3%). It gives a reddish-orange alkaline dithionite vat.

Replacement of Chlorine in 1 : 4-Dichloroanthraquinone.—(*a*) 1 : 4-Dichloroanthraquinone (2 g.), sodium dithionite (2 g.), and 33% ethanolic methylamine (20 ml.) at 140—150° in a sealed tube for 8 hr. gave a product, which on chromatography in chlorobenzene on alumina yielded 1 : 4-dichloroanthraquinone (1·1 g.) and 1-chloro-4-methylaminoanthraquinone (0·14 g., 7·5%), and a trace only of the bismethylamino-derivative.

(*b*) Replacing the dithionite by sodium *m*-nitrobenzenesulphonate, and heating at 155—156°

[10] Steinkopf and Hanske, *Annalen*, 1937, **532**, 241.
[11] Villiger, *Ber.*, 1909, **42**, 3538.

for 8 hr., gave, as above, 1 : 4-dichloro- (0·6 g.), 1-chloro-4-methylamino- (0·16 g., 8·1%), and 1 : 4-bismethylamino-anthraquinone (0·2 g., 10·4%). A similar reaction at 175—180° for 30 hr. gave a similar result, and when pyridine (10 ml.) was added to the mixture (155—165°) the yield of bismethylamino-compound was 0·26 g. (13·5%).

(*c*) 1 : 4-Dichloroanthraquinone (2 g.), copper acetate (0·2 g.), and 33% ethanolic methylamine (20 ml.) at 150—170° in a sealed tube for 20 hr. afforded unchanged product (0·6 g.), 1-chloro-4-methylamino- (0·2 g., 10%), and 1 : 4-bismethylamino-anthraquinone (0·38 g., 19·8%); similar results were obtained at 180—190°.

(*d*) *N*-Methyltoluene-*p*-sulphonamide (11 g.) was heated to 170°, and copper acetate (0·1 g.) and sodium acetate (0·25 g.) were added; when the melt became clear (5 min.), 1 : 4-dichloroanthraquinone (1 g.) was added in portions during 15 min. and the melt then kept at 170° for 6 hr. Addition to water, and extraction of the amide from the solid by dilute sodium hydroxide solutions gave an orange-red insoluble solid, which was dried *in vacuo*, then heated in 95% sulphuric acid (10 ml.) at 60—70° (oil-bath) for 1 hr. Dilution with water afforded a solid, which was dried and chromatographed in chlorobenzene on alumina, to give a deep red band of 1-chloro-4-methylamino- (0·3 g., 30%), m. p. 169°, and a trace of 1 : 4-bismethylamino-anthraquinone, m. p. 220°.

(*e*) 1 : 4-Dichloroanthraquinone (2 g.), toluene-*p*-sulphonamide (3·7 g.), potassium acetate (1·6 g.), and copper acetate (0·1 g.) were refluxed in nitrobenzene (20 ml.) for 4 hr. After removal of nitrobenzene, the residual solid crystallised from acetic acid in orange needles, m. p. 242—243°, of 1 : 4-ditoluene-*p*-sulphonamidoanthraquinone (3·6 g., 90%), hydrolysed almost quantitatively by 95% sulphuric acid on the water-bath in 1 hr. to 1 : 4-diaminoanthraquinone, m. p. 268° (1·6 g.).

8-Chloro-5-toluene-p-*sulphonamido- and 5 : 8-Ditoluene*-p-*sulphonamido-thiophanthrene-4 : 9-quinone.*—5 : 8-Dichlorothiophanthrene-4 : 9-quinone (2 g., 1 mol.), toluene-*p*-sulphonamide (1·9 g., 3 mols.), freshly fused potassium acetate (0·8 g., 2·2 mols), and a trace of copper acetate were refluxed in nitrobenzene (30 ml.) for 4 hr. Nitrobenzene was removed with steam, and the residual reddish-brown solid was crystallised from acetic acid, to yield orange-red plates, m. p. 275—276°, of *5 : 8-ditoluene*-p-*sulphonamidothiophanthrene-4 : 9-quinone* (1·7 g., 44%) (Found : C, 56·5; H, 3·8; N, 5·0; S, 17·4. $C_{28}H_{20}O_6N_2S_2$ requires C, 56·5; H, 3·7; N, 5·1; S, 17·4%). The mother-liquors gave *8-chloro-5-toluene*-p-*sulphonamidothiophanthrene-4 : 9-quinone*, which crystallised from dilute acetic acid in brownish-orange needles, m. p. 181—182° (1·2 g., 40·5%) (Found : C, 54·6; H, 2·4; N, 3·3; Cl, 8·5; S, 15·2. $C_{19}H_{12}O_4NClS_2$ requires C, 54·6; H, 2·9; N, 3·35; Cl, 8·5; S, 15·3%). Chromatography in benzene on alumina proved an excellent means of separating the above derivatives. A longer time of reaction (12 hr.) in the above experiment gave the ditoluene-*p*-sulphonamide (3·6 g., 89%), and only a trace of monotoluene-*p*-sulphonamido-derivative.

5 : 8-Diaminothiophanthrene-4 : 9-quinone.—A solution of 5 : 8-ditoluene-*p*-sulphonamidothiophanthrene-4 : 9-quinone (2·5 g.) and 95% sulphuric acid (20 ml.) was kept at room temperature for 17 hr.; after 2 hr. on the water-bath the mixture was added to water and the solid collected, dried, and crystallised from chlorobenzene in purple needles with a bronze lustre, m. p. >350°, of *5 : 8-diaminothiophanthrene-4 : 9-quinone* (1 g., 97%) (Found : C, 58·8; H, 3·3; N, 11·7; S, 13·0. $C_{12}H_8O_2N_2S$ requires C, 59·0; H, 3·3; N, 11·5; S, 13·1%). The alkaline dithionite vat was bright yellow.

5-Amino-8-chlorothiophanthrene-4 : 9-quinone.—In similar manner hydrolysis of the corresponding sulphonamide (2 g.) gave *5-amino-8-chlorothiophanthrene-4 : 9-quinone* (1·24 g., 98%), which crystallised from benzene in dark red plates with a green lustre, m. p. 227—228° (Found : C, 55·0; H, 2·2; N, 5·3; Cl, 13·4; S, 12·1. $C_{12}H_6O_2NClS$ requires C, 54·7; H, 2·3; N, 5·3; Cl, 13·5; S, 12·2%). It gave a golden-yellow alkaline dithionite vat.

6- and 3-Nitro-2-2′-thenoylbenzoic Acid.—Reaction was carried out in nitrogen. Magnesium turnings (3 g., 1·25 mols.), a crystal of iodine, and a few drops of 2-bromothiophen in dry ether (60 ml.) were heated until reaction began, and then 2-bromothiophen (total, 16·3 g., 1 mol.) was added during 1 hr. under reflux. After refluxing for a further hr. and cooling to 20°, the Grignard reagent was added during 10 min. to a suspension of 3-nitrophthalic anhydride (19·3 g., 1 mol.) in dry benzene (300 ml.) at 40°. The mixture was kept at 50—55° for 2 hr., then water (150 ml.) and magnesium oxide (10 g.) were added, and the mixture was refluxed for 1 hr. Acidification of the aqueous layer and aqueous washings of the solvent layer with acetic acid gave 3-nitro-2-2′-thenoylbenzoic acid, which crystallised from dilute acetic acid in colourless

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needles, m. p. 215—216° (6·85 g., 25%). The filtrate from the acetic acid acidification was made strongly acid by hydrochloric acid, to give the 6-nitro-isomer, which crystallised from dilute acetic acid in colourless prisms, m. p. 168—169° (4·1 g., 14·75%).

8-*Benzamidothiophanthrene*-4 : 9-*quinone*.—A boiling solution of ferrous sulphate (25 g.) in water (165 ml.) which was treated with 28% aqueous ammonia (40 ml.) was added during 5 min. to 3-nitro-2-2′-thenoylbenzoic acid (3·5 g.) in 28% aqueous ammonia (35 ml.). The mixture was boiled for 20 min., filtered, and treated while boiling with a hot solution of potash alum (3·5 g.) in water (35 ml.). After filtering, the solution was cooled to give pale yellow needles, m. p. 176—178°, of 3-amino-2-2′-thenoylbenzoic acid (3 g., 96%). This amine (3 g.) was cyclised by 95% sulphuric acid (50 ml.) for 5 min. at 120°, cooled rapidly to 60°, and added to water (500 ml.). The resulting solid was dried and converted by benzoyl chloride in boiling chlorobenzene (4 hr.) into 8-*benzamidothiophanthrene*-4 : 9-*quinone* which crystallised from chlorobenzene in bright orange needles, m. p. 231—232° (1·9 g., 45·2%, based on nitrocarboxylic acid) (Found : C, 68·4; H, 3·2; N, 3·9; S, 9·2. $C_{12}H_{11}O_3NS$ requires C, 68·5; H, 3·3; N, 4·4; S, 9·6%).

8-*Benzamido- and* 8-*Amino*-5-*chlorothiophanthrene*-4 : 9-*quinone*.—The above 8-benzamido-compound (2 g.) was treated at 100° in nitrobenzene (32 ml.) with sulphuryl chloride (1·5 ml.) for 15 min., with vigorous stirring, then stirred for a further 4 hr. at 100° and at 10° for 1 hr. The light orange crystals were collected, washed with alcohol, and dried. 8-*Benzamido*-5-*chloro-thiophanthrene*-4 : 9-*quinone* crystallised from chlorobenzene in orange, feathery needles, m. p. 225—226° (1·4 g., 63·6%) (Found : C, 62·2; H, 2·7; N, 4·1; S, 9·3. $C_{19}H_{10}O_3NClS$ requires C, 62·0; H, 2·7; N, 3·8; S, 8·7%). Warming with concentrated sulphuric acid on the water-bath for 1 hr. gave the corresponding 8-*amino-derivative*, red plates (from benzene), m. p. 253—254° (Found : C, 55·0; H, 2·4; Cl, 13·4; S, 11·7. $C_{12}H_6O_2NClS$ requires C, 54·7; H, 2·3; Cl, 13·5; S, 12·2%).

5-*Benzamidothiophanthrene*-4 : 9-*quinone*.—A solution of 6-nitro-2-2′-thenoylbenzoic acid (2·5 g.) in 95% sulphuric acid was heated at 140—145° for 2 min., cooled to 60°, and added, with stirring, to water (200 ml.). The cyclised product was extracted with hot sodium carbonate solution to remove unchanged carboxylic acid and then was boiled with sodium dithionite (3 g.), sodium hydroxide (2 g.), and water (200 ml.) for 2 hr. Subsequent aeration for 3 hr. gave a flocculent maroon precipitate, which was collected, washed, and dried; chromatography was effected in chlorobenzene on alumina, to give a reddish-blue band, which was separated with chlorobenzene and then treated with benzoyl chloride. After 4 hours' refluxing and concentration, orange needles, m. p. 229—230°, of 5-benzamidothiophanthrene-4 : 9-quinone, separated (0·75 g., 25%). Chlorination with sulphuryl chloride as above afforded a product containing only 2·7% of chlorine.

2 : 5-*Dimethylthiophen*.—Acetonylacetone (129 g.) and phosphorus pentasulphide (250 g.) were mixed intimately and heated carefully until reaction began; sometimes the reaction began spontaneously and vigorously. After reaction had proceeded, with cooling, for 30 min., the mixture was boiled for a few min. and then distilled. The distillate was washed with dilute hydrochloric acid, water, 10% aqueous sodium carbonate, and finally, water. The resulting liquid was distilled and the fraction, b. p. 132—138° (54 g.), collected.

3 : 6-*Dichloro*-2-(2 : 5-*dimethyl*-3-*thenoyl*)*benzoic Acid* (III).—(*a*) Aluminium chloride (19·6 g., 2·2 mols.) was added during 3 hr. to a mixture of 3 : 6-dichlorophthalic anhydride (14·5 g., 1 mol.), 2 : 5-dimethylthiophen (7·5 g., 1 mol.), and nitrobenzene (45 ml.) at 0—5°. After 20 hours' stirring at room temperature, decomposition with ice and hydrochloric acid, and removal of the nitrobenzene with steam, the tarry residue was extracted with boiling 8% sodium carbonate solution (charcoal); the filtrate from this was acidified with hydrochloric acid; 3 : 6-*dichloro*-2-(2 : 5-*dimethyl*-3-*thenoyl*)*benzoic acid* crystallised from dilute acetic acid in colourless needles, m. p. 172—173° (dried at 120°) (2·9 g., 3·2%) (Found : C, 51·0; H, 3·0; Cl, 21·9; S, 9·8. $C_{14}H_{10}O_3Cl_2S$ requires C, 51·1; H, 2·9; Cl, 21·6; S, 9·7%).

(*b*) 3 : 6-Dichlorophthalic anhydride (14·5 g., 1 mol.), aluminium chloride (19·6 g., 2·2 mols.), and nitrobenzene (35 ml.) were stirred at 55—60° for 1 hr.; 2 : 5-dimethylthiophen (7·5 g., 1 mol.) was added dropwise during 2 hr. at 40—45°, and the mixture was stirred at 40—45° for a further hr. and then at 55—60° for 2 hr. After being stirred at room temperature for 10 hr., the mixture was decomposed by being stirred with water (700 ml.) and hydrochloric acid (10 ml.) for 1 hr. Purification of the resulting product from aqueous sodium carbonate gave a solid, which crystallised from dilute acetic acid in colourless needles, m. p. and mixed m. p. with above

product, 172—173° (9·7 g., 44·3%). The derived *methyl ester* distilled as a colourless oil, b. p. 180—181°/0·4 mm. (Found : C, 52·1; H, 3·1; Cl, 21·0; S, 9·4. $C_{15}H_{12}O_3Cl_2S$ requires C, 52·5; H, 3·5; Cl, 20·7; S, 9·35%).

5 : 8-*Dichloro*-1 : 3-*dimethyl*-β-*thiophanthrene*-4 : 9-*quinone* (IV).—(*a*) **3 : 6**-Dichloro-2-(2 : 5-dimethyl-3-thenoyl)benzoic acid (5 g.) and aluminium chloride (10 g.) in nitrobenzene (75 ml.) were stirred at 130—140° for 24 hr. After decomposition, removal of nitrobenzene with steam, and extraction with boiling aqueous sodium carbonate, the insoluble solid was chromatographed in chlorobenzene on alumina, and gave, after crystallisation from the same solvent, the *quinone* in yellow needles, m. p. 262—263° (2 g., 42·4%). The quinone sublimed readily in stout, yellow needles, m. p. 263—264°, at 200°/0·5 mm. (Found : C, 54·1; H, 2·8; Cl, 22·8; S, 9·9. $C_{14}H_6O_2Cl_2S$ requires C, 54·0; H, 2·6; Cl, 22·8; S, 10·3%). It does not form an alkaline dithionite vat.

(*b*) **3 : 6**-Dichloro-2-(2 : 5-dimethyl-3-thenoyl)benzoic acid (2 g.) was converted by thionyl chloride into its acid chloride, which was then stirred in nitrobenzene (50 ml.) with aluminium chloride (1·8 g., 2·2 mols.) at 120—130° for 6 hr. Subsequent elution, with chlorobenzene, of the yellow band formed on the alumina column gave yellow, feathery needles, 262—263°, of the quinone.

(*c*) The carboxylic acid (2 g.), in a melt of aluminium chloride (12 g.) and sodium chloride (3 g.) at 120—130° for 6 hr. gave, as above, the quinone (IV), m. p. 262° (0·47 g., 25%).

5-Chloro-8-methylamino- and 5 : 8-Dimethylamino-1 : 3-dimethyl-β-thiophanthrene-4 : 9-quinone.—Heating the quinone (IV) (2 g.), 33% ethanolic methylamine (25 ml.), pyridine (10 ml.), and a trace of copper acetate at 135—140° for 8 hr., followed by chromatography in benzene on alumina, gave an orange-red band, quickly eluted; removal of the solvent and crystallisation from light petroleum (b. p. 60—80°) gave orange-red needles, m. p. 197—198°, of ***5-chloro-1 : 3-dimethyl-8-methylamino-β-thiophanthrene-4 : 9-quinone*** (V; R = Cl) (0·2 g., 10·4%) (Found : C, 58·7; H, 4·0; N, 4·4; Cl, 12·0; S, 10·4. $C_{15}H_{12}O_2NClS$ requires C, 58·9; H, 4·0; N, 4·6; Cl, 11·6; S, 10·5%). After elution of the above orange-red band, a royal-blue band remained on the column and was extracted (Soxhlet) with benzene to give, after crystallisation from light petroleum–benzene, purple needles with a coppery lustre, m. p. 247—248°, of **1 : 3-*dimethyl*-5 : 8-*dimethylamino*-β-*thiophanthrene*-4 : 9-*quinone*** (0·54 g., 27·5%) (Found : C, 63·9; H, 5·3; N, 9·1; S, 10·4. $C_{16}H_{16}O_2N_2S$ requires C, 64·0; H, 5·4; N, 9·3; S, 10·7%). This quinone does not form an alkaline dithionite vat. When the time of the above reaction was 16 hr., no chloro-derivative was obtained, and the diamino-derivative was formed in 36·4% yield.

5-Anilino-8-chloro*-1 : 3-*dimethyl*-β-*thiophanthrene*-4 : 9-*quinone*.**—The quinone (IV) (2 g.) and a trace of copper acetate were refluxed in aniline (100 ml.) for 4 hr. After removal of excess of aniline with steam, the maroon product was collected, washed, and dried. Chromatography of the deep red benzene extract on alumina and several crystallisations from light petroleum (b. p. 100—120°) gave maroon needles, m. p. 185°, of ***5-anilino-8-chloro*-1 : 3-*dimethyl*-β-*thiophanthrene*-4 : 9-*quinone (1·2 g., 44%) (Found : C, 65·7; H, 3·8; N, 4·2; Cl, 9·5; S, 8·6. $C_{20}H_{14}O_2NClS$ requires C, 65·3; H, 3·8; N, 3·8; Cl, 9·6; S, 8·7%). It does not form a vat, and dissolves in cold concentrated sulphuric acid with a brownish-orange colour.

3 : 6-Dichloro-2-(5-methyl-2-thenoyl)benzoic Acid.—**3 : 6**-Dichlorophthalic anhydride (43·4 g., 1 mol.), aluminium chloride (58·8 g., 2·2 mols.), and nitrobenzene (100 ml.) were stirred at 55—60° for 1 hr., then cooled to 40—45°. 2-Methylthiophen (19·6 g., 1 mol.) was added dropwise during 1½ hr. at 40—45°; heating was continued at 40—45° for 1 hr., then at 50—60° for 4 hr., the colour changing from blood-red to purple. After being stirred overnight at room temperature, the mixture was decomposed, nitrobenzene removed with steam, and the residue extracted with boiling 8% sodium carbonate solution. Acidification of the alkaline extract, followed by crystallisation of the resulting solid from dilute acetic acid, gave colourless prisms, m. p. 160—161°, of ***3 : 6-dichloro-2-(5-methyl-2-thenoyl)benzoic acid*** (36 g., 57·1%) (Found : C, 49·6; H, 2·5; Cl, 22·5; S, 10·2. $C_{13}H_8O_3Cl_2S$ requires C, 49·5; H, 2·6; Cl, 22·5; S, 10·2%). The *methyl ester* (Fischer–Speier) crystallised from methanol in colourless rhomboids, m. p. 97—98° (Found : C, 50·7; H, 2·8; Cl, 21·9; S, 9·3. $C_{14}H_{10}O_3Cl_2S$ requires C, 51·1; H, 3·1; Cl, 21·6; S, 9·7%). Attempted cyclisation of the carboxylic acid or its chloride by aluminium chloride in nitrobenzene at 120—130° for 20 hr., by aluminium–sodium chloride at 130° for 8 hr., or by phosphoric oxide in nitrobenzene at 130—140° for 24 hr., gave intractable products.

3 : 6-Dichloro-2-(5-methyl-2-thenyl)benzoic Acid (VI).—**3 : 6**-Dichloro-2-(5-methyl-2-thenoyl)-benzoic acid (10 g.), 28% aqueous ammonia (500 ml.), copper sulphate (0·25 g.), and zinc dust

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(25 g.) were refluxed for 40 hr., and 28% aqueous ammonia (50 ml.) added every 12 hr. The suspension was filtered hot, and the filtrate acidified; on cooling, an oil separated, which became solid after several days. Several crystallisations from dilute acetic acid afforded colourless plates, m. p. 107—108°, of the *thenyl derivative* (V), which were dried at 100° for 24 hr. (4·5 g., 47·4%) (Found: Cl, 23·0; S, 10·2. $C_{13}H_{10}O_2Cl_2S$ requires Cl, 23·55; S, 10·6%).

4-*Acetoxy*-5 : 8-*dichloro*-2-*methylthiophanthrene* (V).—The above thenyl derivative (2 g.), acetic anhydride (8 ml.), acetic acid (12 ml.), and freshly fused zinc chloride (0·5 g.) were refluxed for 90 min. to give a clear solution; dilution with hot water (20 ml.) afforded a solid which crystallised from acetic acid in feathery, colourless needles, m. p. 191°, of the *acetoxy-compound* (2·1 g., 96%) (Found: C, 55·3; H, 3·1; Cl, 21·6; S, 9·6. $C_{15}H_{10}O_2Cl_2S$ requires C, 55·4; H, 3·1; Cl, 21·8; S, 9·9%).

5 : 8-*Dichloro*-2-*methylthiophanthrene*-4 : 9-*quinone* (VIII).—The acetoxy-compound (2 g.) was refluxed in acetic acid (20 ml.) with potassium dichromate (8 g.) for 1 hr., the mixture filtered, and the filtrate concentrated to 8 ml. and added to water (100 ml.). The yellow flocculent precipitate was collected, dried, crystallised three times from acetic acid, and sublimed at 200°/0·5 mm., to give bright yellow needles, m. p. 238°, of **5 : 8-*dichloro*-2-*methylthiophanthrene*-4 : 9-*quinone*** (VIII) (1·5 g., 82%) (Found: C, 52·9; H, 2·0; Cl, 23·8; S, 10·7. $C_{15}H_6O_2Cl_2S$ requires C, 52·5; H, 2·0; Cl, 23·9; S, 10·8%). It forms a reddish-orange alkaline dithionite vat.

5 : 8-*Dianilino*-2-*methylthiophanthrene*-4 : 9-*quinone*.—5 : 8-Dichloro-2-methylthiophanthrene-4 : 9-quinone (1 g.) was refluxed in aniline (70 ml.) with a little copper acetate for 4 hr., a deep blue solution resulting. Aniline was removed with steam, the dark residue extracted with benzene, and the greenish-blue extract chromatographed on alumina. A faint blue band preceded an intense bluish-green one, and was separated from a dark brown band of impurities by elution with benzene. The bluish-green band gave the *anilino-derivative* in dark blue crystals [from light petroleum (b. p. 60—80°)], m. p. 176—177° (0·5 g., 36%) (Found: N, 7·0. $C_{25}H_{16}O_2N_2S$ requires N, 6·8%).

3 : 6-*Dichloro*-2-(3-*methyl*-2-*thenoyl*)*benzoic Acid* (IX).—3 : 6-Dichlorophthalic anhydride (21·7 g., 1 mol.) was treated (Friedel–Crafts) with 3-methylthiophen (9·8 g., 1 mol.), under similar conditions to those recorded for 2-methylthiophen, to yield the *acid* (IX) (20·4 g., 64·8%); five crystallisations from dilute acetic acid gave colourless prisms of constant m. p. 164—165° (Found: C, 49·5; H, 2·4; Cl, 22·6; S, 10·2. $C_{13}H_8O_3Cl_2S$ requires C, 49·5; H, 2·6; Cl, 22·5; S, 10·2%). The *methyl ester* (Fischer–Speier) crystallised from methanol in colourless rhomboids, m. p. 107—108° (Found: C, 51·1; H, 2·9; Cl, 21·8; S, 9·5. $C_{14}H_{10}O_3Cl_2S$ requires C, 51·1; H, 3·1; Cl, 21·6; S, 9·7%).

Cyclisation. The acid (IX) (4 g.) was added slowly to aluminium chloride (24 g.) and sodium chloride (6 g.) at 130—135°, and kept at this temperature for 10 hr. before being added to ice and water. After extraction with boiling 8% aqueous sodium carbonate, the residue was dried and chromatographed in chlorobenzene on alumina; a yellow band separated from the main diffuse dark brown band, and the former gave a solid which crystallised from acetic acid in brownish-yellow needles, m. p. 272—273° (0·08 g., 2·1%), of, probably, **5 : 8-*dichloro*-3-*methylthiophanthrene*-4 : 9-*quinone*** (X) (Found: C, 53·1; H, 2·5; Cl, 23·1; S, 10·8. $C_{15}H_6O_2Cl_2S$ requires C, 52·5; H, 2·0; Cl, 23·9; S, 10·8%). Other methods of cyclisation gave no quinone. The alkaline dithionite vat was orange-brown.

3 : 6-*Dichloro*-2-(3-*methyl*-2-*thenyl*)*benzoic Acid*.—The thenoyl derivative (IX) (10 g.) was reduced by refluxing with zinc dust (25 g.), copper sulphate (0·25 g.), and 28% aqueous ammonia (500 ml.) for 40 hr., 28% aqueous ammonia being added at intervals. The hot mixture was filtered and the filtrate acidified with hydrochloric acid, to give a solid; crystallisatilon from dilute acid afforded colourless, rod-like needles, m. p. 178—179°, of **3 : 6-*dichloro*-2-(3-*methyl*-2-*thenyl*)*benzoic acid*** (5·5 g., 57·5%) (Found: C, 52·1; H, 3·4; Cl, 23·7; S, 10·4. $C_{13}H_{10}O_2Cl_2S$ requires C, 51·8; H, 3·3; Cl, 23·55; S, 10·6%).

This compound (2 g.), zinc chloride (0·15 g.), acetic acid (12 ml.), and acetic anhydride (8 ml.) were refluxed for 90 min., the solution becoming blood-red; dilution with water (25 ml.) and cooling gave a red solid, which was extracted with acetic acid (charcoal); the acid was then filtered, diluted with water, and cooled, to give colourless needles, m. p. 241—242°. The needles were soluble in aqueous sodium hydrogen carbonate, indicating that this was not a cyclised product; boiling with aqueous sodium hydroxide gave unchanged material. Analyses supported the view that it was **2-(5-*acetyl*-3-*methyl*-2-*thenyl*)-3 : 6-*dichlorobenzoic acid***

(Found : C, 52·5; H, 3·7; Cl, 21·2; S, 8·9. $C_{15}H_{12}O_3Cl_2S$ requires C, 52·5; H, 3·5; Cl, 20·7; S, 9·3%). The dark residue from the acetic acid extraction above proved intractable.

2-Iodo-3-methylthiophen.—2-Chloromercuri-3-methylthiophen [9] (11·2 g.), iodine (8·6 g.), and potassium iodide (20 g.) in water (150 ml.) were stirred at room temperature for 6 hr. and left overnight. Decolorisation was affected by aqueous sodium hydrogen sulphite, and the mixture distilled with steam, to yield a pale yellow oil; extraction with ether, washing the extract with aqueous sodium hydrogen sulphite and then water, and drying, gave on distillation a pale yellow oil, b. p. 84—86°/11 mm., of 2-iodo-3-methylthiophen.[10]

Synthesis of 3 : 6-*Dichloro*-2-(3-*methyl*-2-*thenoyl*)*benzoic Acid.*—Preparation of the Grignard reagent, and the condensation, were carried out in pure dry nitrogen. Magnesium (0·8 g., 1·25 mols.), a crystal of iodine, and a little 2-iodo-3-methylthiophen in dry ether (60 ml.) were warmed until reaction began, and then 2-iodo-3-methylthiophen (total, 6·0 g., 1 mol.) was added during 30 min. and the mixture refluxed for 1 hr. To a solution of 3 : 6-dichlorophthalic anhydride (5·8 g., 1 mol.) in dry benzene (180 ml.) at 50°, the Grignard solution was pumped in during 3 min., the temperature rising to 55°. After 1 hr. at 55° water (150 ml.) was added and the mixture refluxed for 1 hr. After cooling, magnesium oxide (1·2 g.) was added and the mixture shaken at 25° for 3 hr. The aqueous layer, and aqueous washings of the benzene layer, were acidified; the resulting solid crystallised from dilute acetic acid in colourless plates, m. p. 163° (4·2 g., 50%). No depression in m. p. was observed on admixture with the product obtained from 3-methylthiophen by the Friedel–Crafts reaction. Further, conversion into the methyl ester gave colourless rhomboids, m. p. and mixed m. p. with the methyl ester obtained previously, 107—108°.

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CLOTHWORKERS' RESEARCH LABORATORY,
THE UNIVERSITY, LEEDS.

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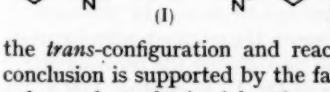
293. *ω-Halogenomethyl-pyridines, -quinolines, and* -isoquinolines. *Part VI.*[1] *Compounds related to* 1 : 2-*Di*-2′-*quinolylethylene.*

By I. M. C. BARFOOT, D. LL. HAMMICK, E. D. MORGAN, and A. M. ROE.

The reactions of some non-planar halogenated diquinolylethylenes are described, and, for the principal members of the series, configurations are assigned and dipole moments recorded.

IN Part V [1] we described the preparation of two stereoisomers of 1 : 2-di-2′-quinolylethylene (I; X = H) and of its dichloro- and dibromo-analogues (I; X = Cl, Br). On the evidence of the ultraviolet spectra we assigned the *trans*-configuration to the more stable β-1 : 2-di-2′-quinolylethylene. The present paper is concerned with the elucidation of the stereochemistry of the halogenoethylenes and with the preparation of some additional compounds of this series.

ωωω-Tribromoquinaldine reacts with copper in boiling pyridine to give a mixture of β-1 : 2-dibromo-1 : 2-di-2′-quinolylethylene (I; X = Br) and 1 : 2-di-2′-quinolylacetylene. The same reaction with ωωω-trichloroquinaldine has afforded only β-1 : 2-dichloro-1 : 2-di-2′-quinolylethylene (I; X = Cl). A comparative study of the dehalogenation with copper in boiling pyridine of the isomeric dihalogenoethylenes has shown that the α-isomers give the acetylene very much more readily than do the β-isomers. We take this to mean that the α-isomers have the *trans*-configuration and react by a *trans*-elimination of the halogen atoms.[2] This conclusion is supported by the fact that α-1 : 2-dibromo-1 : 2-di-2′-quinolylethylene is the only product obtained by the action of bromine on 1 : 2-di-2′-quinolylacetylene.



(I)

[1] Part V, Hammick, Lammiman, Morgan, and Roe, *J.*, 1955, 2436.
[2] Crombie, *Quart. Rev.*, 1952, **6**, 130; Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953, p. 465.

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The debromination of 1 : 2-dibromo-compounds by the action of copper in pyridine is probably a stereospecific *trans*-elimination. When 1 : 2-dibromo-1 : 2-di-2′-quinolylethane, made by the presumably *trans*-addition of bromine to the *trans*-ethylene, is treated with copper in pyridine, *trans*(or β)-1 : 2-di-2′-quinolylethylene is isolated in 69% yield. The methods of preparation and all the physical and chemical properties of each pair of isomeric dihalogenoethylenes are comparable: thus, the higher-melting, less soluble α-isomers are obtained by irradiation of the β-isomers, and absorb less strongly in the ultraviolet region. For this reason we conclude, by analogy with the corresponding debromination reactions, that the relatively rapid dechlorination of α-1 : 2-dichloro-1 : 2-di-2′-quinolylethylene is also a *trans*-elimination.

The relative stability of the isomeric dibromoethylenes under various conditions has been studied. Treatment of each isomer with a catalytic quantity of iodine in boiling pyridine did not cause isomerisation; in nitrobenzene, however, equilibration appeared to occur along with much decomposition. Treatment of the α-isomer with potassium hydroxide in boiling methanol gave the β-isomer. This lower stability of the α-isomer may be due to the fact that in the *trans*-configuration neither quinoline ring can, owing to the size of the bromine atoms, lie in the same plane as the ethylenic bond. However, in the *cis*-configuration *one* of the quinoline rings can conjugate with the ethylenic bond: this may be related to the similar, but more intense, ultraviolet absorption of the β(or *cis*)-isomer.

This argument may be further pursued in the case of the new compounds obtained by the action of the halogen acids on 1 : 2-di-2′-quinolylacetylene. Whereas the β-ethylene is stable to prolonged treatment with 2N-hydrochloric acid, the acetylene readily furnishes 1-chloro-1 : 2-di-2′-quinolylethylene. Hydrobromic acid gives, less readily, 1-bromo-1 : 2-di-2′-quinolylethylene. The action of hydriodic acid on the acetylene produced β-1 : 2-di-2′-quinolylethylene and a compound melting at 102—103°, which readily lost iodine.

In passing from the unsubstituted ethylene to the dihalogenated ethylenes we have found that the order of stability shifts from the *trans*- to the *cis*-isomer, apparently because of the steric effect of the halogen atoms. In the monohalogenated ethylenes an intermediate state is found, where the *trans*- are only slightly more stable than the *cis*-forms. Addition of hydrogen chloride to diquinolylacetylene gave *trans*-1-chloro-1 : 2-di-2′-quinolylethylene together with a trace of the *cis*-isomer (identified by its ultraviolet spectrum). Addition of hydrogen bromide gives *trans*-1-bromo-1 : 2-di-2′-quinolylethylene, contaminated with larger amounts of the *cis*-isomer. The *trans*-isomer crystallises more readily from light petroleum or benzene, and is eluted more readily when the mixture is chromatographed on a column of alumina prepared in carbon tetrachloride; pure isomers, however, have not been isolated.

Thus there is a gradual diminution in the relative stabilities of the *trans*-isomers in the series 1 : 2-diquinolyl-, 1-chloro-1 : 2-diquinolyl-, 1-bromo-1 : 2-diquinolyl-, to the 1 : 2-dichloro- and 1 : 2-dibromo-1 : 2-diquinolyl-ethylenes, which are of comparable stability.

1-Chloro- and 1-bromo-1 : 2-di-2′-quinolylethylene have been treated with chlorine and bromine respectively to give the corresponding 1 : 1 : 2-trihalogeno-1 : 2-di-2′-quinolylethanes.

An attempt has been made to prepare the α(or *cis*)-1 : 2-di-2′-quinolylethylene by catalytic reduction of a dibromoethylene or from diquinolylacetylene.[3] With a palladium on strontium carbonate catalyst in the presence of potassium hydroxide[4] both isomeric dibromoethylenes gave the same β(or *trans*-)1 : 2-di-2′-quinolylethylene. In the case of the β(or *cis*)-dibromoethylene isomerisation occurs; the same thing apparently happens during the reduction of 1 : 2-di-2′-quinolylacetylene which also affords the *trans*-olefin.[5]

Dipole moments were made available by the kindness of Dr. L. E. Sutton, F.R.S., in

[3] Cf. Ahmad, Bumpus, and Strong, *J. Amer. Chem. Soc.*, 1948, **70**, 3391.
[4] Cf. Busch and Stove, *Ber.*, 1916, **49**, 1063.
[5] Cf. Bourguel, *Bull. Soc. chim. France*, 1929, **45**, 1067.

whose laboratory they were measured by Mr. C. J. M. Cutcliffe. The figures in the Table are in accordance with the above assignments.

Dipole moments (D) (Q = 2-quinolyl).

trans-Q·CH:CH·Q	1·60		
trans-Q·CCl:CCl·Q	1·54	*trans*-Q·CBr:CBr·Q	1·36
cis-Q·CCl:CCl·Q	4·87	*cis*-Q·CBr:CBr·Q	4·68

Experimental

Debromination of ωωω-*Tribromoquinaldine.*—ωωω-Tribromoquinaldine (20 g.) in pyridine (40 ml.) was added during 1 hr. to a stirred refluxing mixture of pyridine (60 ml.) and copper bronze powder (10 g.). The stirred mixture was refluxed for a further 0·5 hr., then water (1 l.) was added after cooling. The solid was collected next day, washed with aqueous ammonia (*d* 0·880) and water, and dried. The organic material was dissolved in the minimum quantity of benzene–carbon tetrachloride (1 : 1) and chromatographed on alumina; elution with the same solvent gave β-1 : 2-dibromo-1 : 2-di-2′-quinolylethylene (2·9 g., 28%) as pale yellow needles [from light petroleum (b. p. 80—100°)], m. p. 142 —143°. Elution with benzene–ether (1 : 1) gave 1 : 2-di-2′-quinolylacetylene (3 g., 40%), m. p. 179—180°.

Dehalogenation of 1 : 2-*Dihalogeno*-1 : 2-*di*-2′-*quinolylethylenes.*—The dehalogenations described [1] were carried out under standard conditions with various periods of reflux. A summary of results obtained is given.

	Q·CX:CX·Q (Q = 2-quinolyl)					
	X = Br			X = Cl		
	α-	β-		α-	β-	
Time (min.)	25	60	1080	60	60	1080
Recovered ethylene (%)	—	68	—	—	50	—
Yield of acetylene (%)	52	—	34	38	—	—

Debromination of 1 : 2-*Dibromo*-1 :·2-*di*-2′-*quinolylethane.*—1 : 2-Dibromo-1 : 2-di-2′-quinolylethane, prepared from β-1 : 2-di-2′-quinolylethylene by the method of Walker *et al.*,[6] had m. p. 172—173°.

Copper bronze powder (0·2 g.) was slowly added to 1 : 2-dibromo-1 : 2-di-2′-quinolylethane (0·34 g.) in pyridine (20 ml.). The mixture was boiled under reflux for 3 hr., cooled, and poured into ice and water. Next day the solid was collected and washed with ammonia (*d* 0·880) and water. The dried residue crystallised from light petroleum (b. p. 80—100°) to give colourless needles of β-1 : 2-di-2′-quinolylethylene (0·15 g., 69%), m. p. and mixed m. p. 192—193°.

1-*Chloro*-1 : 2-*di*-2′-*quinolylethylene.*—1 : 2-Di-2′-quinolylacetylene (2 g.) was boiled in 2N-hydrochloric acid (100 ml.) for 6 min. and while still hot was poured into 2N-ammonia. The precipitated solid was purified on alumina in benzene–carbon tetrachloride (1 : 1) and crystallised from light petroleum (b. p. 80—100°) to give 1-*chloro*-1 : 2-*di*-2′-*quinolylethylene* as white needles, m. p. 110° (Found : C, 75·6; H, 4·1; N, 9·0; Cl, 11·2. $C_{20}H_{13}N_2Cl$ requires C, 75·6; H, 4·1; N, 8·8; Cl, 11·2%), $\lambda_{max.}$ 2725 3450 (ε 49,500 36,000). The *dipicrate* separated as yellow plates, m. p. 235—236°, from boiling methanol (Found : C, 49·4; H, 2·7; N, 14·1; Cl, 5·0. $C_{32}H_{19}O_{14}N_8Cl$ requires C, 49·6; H, 2·5; N, 14·4; Cl, 4·6%).

When β-1 : 2-di-2′-quinolylethylene was treated with 2N-hydrochloric acid the only product isolated was β-1 : 2-*di*-2′-*quinolylethylene dihydrochloride*, which separated from hot water as colourless needles, m. p. 249—250° (decomp.) (Found : C, 66·4; N, 4·8; N, 7·9; Cl, 20·4. $C_{20}H_{16}N_2Cl_2$ requires C, 67·6; H, 4·5; N, 7·9; Cl, 20·0%).

1-*Bromo*-1 : 2-*di*-2′-*quinolylethylene.*—1 : 2-Di-2′-quinolylacetylene (1·5 g.) was boiled for 15 min. in hydrobromic acid (40 ml.; 25% w/w) and while hot was poured into 2N-ammonia. Three crystallisations of the precipitated solid from light petroleum (b. p. 80—100°) gave 1-*bromo*-1 : 2-*di*-2′-*quinolylethylene* (1·3 g.) as lemon-yellow prisms, m. p. 115—116° (Found : C, 66·0; H, 3·6; N, 7·9; Br, 22·4. $C_{20}H_{13}N_2Br$ requires C, 66·4; H, 3·6; N, 7·8; Br, 22·2%), $\lambda_{max.}$ 2725 3400 (ε 40,000 26,800). The *dipicrate* (from boiling methanol) had m. p. 211—212° (Found : C, 47·2; H, 2·7; N, 13·9; Br, 10·2. $C_{32}H_{19}O_{14}N_8Br$ requires C, 46·9; H, 2·3; N, 13·9; Br, 9·8%).

1 : 1 : 2-*Trichloro*-1 : 2-*di*-2′-*quinolylethane.*—1-Chloro-1 : 2-di-2′-quinolylethylene (0·5 g.) in dry boiling carbon tetrachloride (100 ml.) was treated with chlorine for 30 min. After excess of

[6] Walker, Baldwin, Thayer, and Corson, *J. Org. Chem.*, 1951, **16**, 1805.

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chlorine had been boiled off, the cold solution was washed with aqueous ammonia and evaporated. The residue crystallised from light petroleum and was twice recrystallised from acetone–water to give 1 : 1 : 2-*trichloro*-1 : 2-*di*-2′-*quinolylethane* (0·2 g.) as fine white prisms, m. p. 138—139°, resolidifying to melt again at 187—190° (Found: C, 61·9; H, 3·4; N, 7·1; Cl, 27·5. $C_{20}H_{13}N_2Cl_3$ requires C, 61·8; H, 3·4; N, 7·1; Cl, 27·9%).

1 : 1 : 2-*Tribromo*-1 : 2-*di*-2′-*quinolylethane*.—1-Bromo-1 : 2-di-2′-quinolylethylene (0·4 g.) in dry carbon tetrachloride (50 ml.) was refluxed with bromine (0·4 ml.) for 10 min. The carbon tetrachloride was removed and the residue treated with dilute aqueous ammonia. Recrystallisation of the product from light petroleum (b. p. 60—80°) containing a little benzene, followed by recrystallisation from acetone–water, gave white prisms of 1 : 1 : 2-*tribromo*-1 : 2-*di*-2′-*quinolylethane*, m. p. 150—151° (decomp.) (Found: C, 46·1; H, 2·7; N, 5·3; Br, 45·6. $C_{20}H_{13}N_2Br_3$ requires C, 46·1; H, 2·5; N, 5·4; Br, 46·0%).

Reduction of α-1 : 2-*Dibromo*-1 : 2-*di*-2′-*quinolylethylene*.—α-1 : 2-Dibromo-1 : 2-di-2′-quinolylethylene (0·4 g.) in dry methanol (25 ml.) and dioxan (25 ml.) containing potassium hydroxide (0·1 g.) and pre-reduced palladium on strontium carbonate (0·1 g.) was shaken under hydrogen. Absorption of hydrogen (11 c.c. at 18°/700 mm. Calc. for 2H: 10 c.c.) ceased after 10 min. The solution was filtered and evaporated under reduced pressure; crystallisation of the residue from benzene gave β-1 : 2-di-2′-quinolylethylene (0·12 g., 94%), m. p. and mixed m. p. 185—186°.

Reduction of β-1 : 2-*Dibromo*-1 : 2-*di*-2′-*quinolylethylene*.—β-1 : 2-Dibromo-1 : 2-di-2′-quinolylethylene (1 g.) in dry methanol (100 ml.) containing potassium hydroxide (0·2 g.) and pre-reduced palladium on strontium carbonate (0·2 g.) was shaken under hydrogen. Absorption of hydrogen (62 c.c. at 23°/744 mm. Calc. for 2H: 59 c.c.) ceased after 15 min. β-1 : 2-Di-2′-quinolylethylene was isolated as above.

Reduction of 1 : 2-*Di*-2′-*quinolylacetylene*.—The diquinolylacetylene (0·5 g.) in dry ethyl acetate (20 ml.) containing pre-reduced palladium on strontium carbonate (0·2 g.) was shaken under hydrogen. Absorption of hydrogen (49 c.c. at 23°/740 mm. Calc. for 2H: 47 c.c.) ceased after 15 min. β-1 : 2-Di-2′-quinolylethylene was isolated as before.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, October 24th*, 1956.]

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294. *The Analysis of Rotatory Dispersion*: 1 : 2-*Diphenylethanol*.

By M. K. HARGREAVES.

The equilibrium method of analysis has been applied to the rotation–temperature curves of 1 : 2-diphenylethanol. The value of ΔH so obtained is in agreement with that obtained by calorimetric measurements. The results show that, in certain cases, the experimental accuracy required for a successful analysis may be quite moderate.

GERRARD and KENYON [1] examined the rotatory dispersion of 1 : 2-diphenylethanol at different temperatures in the homogeneous state and in various solvents. Application of the equilibrium method of analysis [2] to these results for the homogeneous material is recorded below.

ANALYSIS

Examination of the $[\alpha]$–T curves for the different wavelengths suggests, in the light of the findings with 2 : 3-epoxypropyl phenyl ether,[2] that only one of these curves (that for 5461 Å) should be analysable by this method into the rotatory constant of two isomeric forms or conformations. This curve is, in fact, the only one in which all the points lie on a smooth line to within the accuracy previously thought to be required. The result obtained for this line is, therefore, the most probable ($\Delta H = 5{\cdot}85$ kcal./mole). The analysis for the other curves was carried out merely to see whether an analysis was possible. Reasonable solutions were obtained for all except that for 4358 Å. For λ 6708 Å a straightforward solution was obtained from a smoothed

[1] Gerrard and Kenyon, *J.*, 1928, 2564.
[2] Hargreaves, *J.*, 1957, 1071.

curve even though two of the points lie off the curve by as much as 0·5°. In the case of 2 : 3-epoxypropyl phenyl ether curves of this kind were found to be useless. The difference in the sensitivity in the two cases lies in the form of the $[\alpha]$–T curve. In 2 : 3-epoxypropyl phenyl ether the change of $d[\alpha]/dT$ with T is so small in the visible region, over the range of temperature covered, that certain terms in the solution are reduced nearly to zero, so that the expression becomes unusable. For homogeneous 1 : 2-diphenylethanol all the terms are of sufficient magnitude; even in this case, however, a smooth curve through the points for 4358 Å does not yield a solution. It seems possible that these readings are in error as the slope of the $[\alpha]$–T curve is quite different from those for the other wavelengths. Although by suitable minor adjustments in the values taken, solutions from this line are also possible, as has been pointed out previously,[2] the justification of the method lies in the coherence of the values obtained directly from a smooth curve through the experimental points.

The temperatures in the earlier paper were recorded only to the nearest degree; the success of these solutions implies that in most cases the temperatures were more accurate than claimed.

Wavelength (Å)		$[\alpha]_1$	$[\alpha]_2$	$[\alpha]_3$	$[\alpha]_4$	a	b	ΔH	ΔS
		$[\alpha]_1'$	$[\alpha]_2'$	$[\alpha]_3'$	$[\alpha]_4'$				
5461	{	31·82°	20·40°	(13·05)°	6·51°	−5·47	111·2	5·85	19·1
	{	31·82	20·40	16·57	(8·97)				
6708	{	20·20	12·85	(7·83)	3·41	−4·69	61·17	6·02	19·1
	{	20·20	12·85	10·32	(5·19)				
5893	{	26·11	16·80	(10·40)	(4·90)	−3·64	64·08	6·95	22·4
	{	26·11	16·80	13·39	(6·95)				
5780	{	27·88	17·68	(11·25)	5·22	−8·56	160·2	4·71	16·7
	{	27·88	17·68	14·38	(7·50)				
4358		No satisfactory solution.							

The Table gives values for the specific rotations used in solving, by the previous method,[2] the equilibrium relation, $(b - [\alpha]_2^T)/([\alpha]_1^T - a) = \exp(-\Delta H/\boldsymbol{R}T + \Delta S/\boldsymbol{R})$. The values of $[\alpha]$ used are those given by Gerrard and Kenyon,[1] those in parentheses being interpolated from a smooth curve through the experimental points. a and b are the rotatory constants of two forms A and B in the equilibrium B ⇌ A. The form B is that predominating at low temperatures. The experimental temperatures were given to the nearest degree (c). The temperatures (K) corresponding to the values of $[\alpha]$ are: T_1 333·16; T_2 353·16; T_3 372·92; T_4 398·16: T_1' 333·16; T_2' 353·16; T_3' 363·16; T_4' 387·05.

Discussion

The heats of dilution of 1 : 2-diphenylethanol in the solvents used for the dispersion measurements have been determined, and an attempt has been made to correlate the dispersion and thermochemical measurements.[3] The heat of dilution measures the algebraic sum of the changes in the heat content of the system during dilution due to the breaking and the formation of solute–solute, solvent–solvent, and solute–solvent "bonds." It also includes any heat exchange due to changes in conformational potential energy. Since the barrier which restricts free rotation about a single bond corresponds to about 3 kcal./mole, the energy differences between different energy troughs (or different conformations) will be less than this. The substitution of a methyl group for one of the hydrogen atoms in ethane raises [4] the energy barrier by about 0·5 kcal./mole. The differences in energy between different conformations may, therefore, be expected to be of this order, where no bonding exists, and may be neglected, to a first approximation, in comparison with energy changes due to the formation of bonds. In the dilution of 1 : 2-diphenylethanol with benzene, and possibly also with carbon tetrachloride and carbon disulphide, it is reasonable to assume that the observed heat changes are due solely to the rupture of solute–solute "bonds." In the attempt to explain the dispersion, a "tied" form of the molecule was proposed for the solution in ethanol and in the cold homogeneous state, this form being distinct from a free, non-hydrogen bonded form, and from one in which any bonding does

[3] Hargreaves, *J.*, 1954, 1233.
[4] Coulson, "Valence," Oxford, 1952, p. 314.

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not give rise to an element of " structure " in the solution. The equilibrium method of analysis may thus be applied to these postulated forms of 1 : 2-diphenylethanol. The difference between the heat content of the forms predominating at high temperatures and that of the form prevalent at low temperatures may consist only in the breaking of " bonds " between like molecules, and in conformational energy changes. It is interesting that the heat-content change calculated on this basis is of similar magnitude to the heat of dilution in a non-polar solvent, *e.g.*, benzene or carbon tetrachloride. Since 1 : 2-diphenylethanol is monofunctional, *i.e.*, it can undergo change or association only through its single hydroxyl group, this relation is to be expected.

The correlation between the most probable value from the Table, $\Delta H = 5{\cdot}85$ kcal./mole, and the heat of dilution, 5·7 kcal./mole in carbon tetrachloride and 5·2 kcal./mole in benzene, is very satisfactory, the differences being of the order of the experimental error in the thermochemical experiments.

The values obtained for ΔS are in agreement with the suggestion that the low-temperature form is a hydrogen-bridged state. The large value of the entropy change suggests a considerable loosening of the " structure " of the solution in attaining the high-temperature form. The calculations involved are such, however, that at present it would be unwise to place much reliance on the magnitude of the values of ΔS so obtained.

Values and Dispersion of the Rotatory Constants.—The rotatory constant a obtained by this analysis is too small to account for the observed rotations in carbon disulphide, chloroform, and pyridine, though in agreement with the values observed in benzene and carbon tetrachloride. It seems likely, however, from the dilution experiments, that some kind of association complex or compound is formed between 1 : 2-diphenylethanol and chloroform or pyridine, so that the rotatory power observed in these solvents is not strictly that of 1 : 2-diphenylethanol itself. In carbon disulphide, on the other hand, there is no suggestion from the heat of dilution that complex formation occurs, yet the value of α is greater than a. The whole range of observed rotations of the solute under different conditions should lie between the value of a and that of b. Compared with the experimental values in different solvents,[1] the values of a given in the Table are too low by as much as a half. As was pointed out previously,[2] the values of these rotatory constants are more susceptible to error than are ΔH or ΔS. The values of a and of b obtained from the different wavelengths vary widely, so it is useless to consider their dispersion. However, by using the most probable value of ΔH and ΔS it is possible to calculate a and b for each wavelength from the rotation at any two temperatures. By using 333·16° K and 363·16° K the following values are obtained :

λ (Å)	a	b	λ (Å)	a	b
6708	−3·14	69·84	5461	−4·21	108·5
5893	−3·94	90·03	4358	(−1·65)	(197·1)
5780	−4·01	95·71			

Although the magnitudes of these values are probably incorrect their dispersion is of some interest. Results for 4358 Å (see above) being neglected, the b values show pseudosimple dispersion, the straight-line plot of $1/b$ against λ^2 giving an intercept on the λ^2 axis corresponding to λ_0 1900 Å. The plot of $1/a$ against λ^2 giving a straight line and a negative value of λ_0^2. The apparent dominance of the " phenyl band " [3] at low temperatures and in alcoholic solution corresponds to the interaction of two dispersions with low values of λ_0. The preponderance of the B form corresponds to the apparent dominance by the longer waveband. The lower rotatory strength of a than of b may be due to the possibility of the orientation of the benzene nuclei in the " free " form in such a way that their contributions to the rotatory strengths nearly cancel one another.

QUEEN ELIZABETH COLLEGE, UNIVERSITY OF LONDON,
CAMPDEN HILL ROAD, LONDON, W.8.

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295. *Oxidation of Organic Sulphides. Part VIII.*[1] *Autoxidation of Thiacyclohexane, 2-Ethyl-2-methyl-5-isopropylthiacyclopentane, and Thiacyclohex-3-ene.*

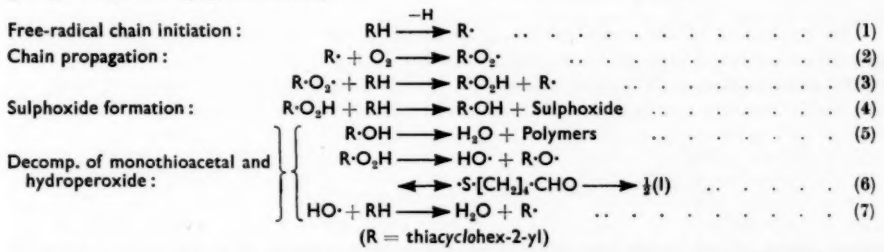
By L. Bateman, J. I. Cunneen, and J. Ford.

The above-named cyclic sulphides react with oxygen by mechanisms similar to those advanced previously for their respective acyclic analogues. A practical point of difference is that in reactions involving rupture of C–S bonds, the products produced in the latter systems are replaced in the former by "dimeric" products arising from ring opening and subsequent combination of RS· radicals.

In Parts IV [2] and VII [1] the reaction of oxygen with certain saturated and unsaturated acyclic sulphides was described, and reaction mechanisms were postulated which were consistent both with the complex product and kinetic data and with independent information on hydroperoxide–sulphide interactions.[3] These studies have now been extended to cyclic sulphides, since these structures occur in ordinary vulcanized rubber [4] whose autoxidation is of great technological importance.

Inert by itself, thia*cyclo*hexane reacts readily with oxygen at moderate temperatures in the presence of catalytic amounts of azo*iso*butyronitrile to produce water and sulphoxide groups in yields which vary little with the extent of reaction—features previously found to be characteristic of saturated acyclic sulphides.[1] The sulphoxide groups are located wholely in thia*cyclo*hexane oxide, and the other main reaction product is the dialdehydic disulphide (I), which was characterized by the formation of a bis-2 : 4-dinitrophenylhydrazone, and by reduction to 5-mercaptopentan-1-ol on treatment with lithium aluminium hydride.

The disulphide (I) has no parallel in the oxidation products of acyclic sulphides, but its formation is readily explained by a series of reactions analogous to that postulated for *n*-butyl methyl sulphide,[1] with the logical difference that the derived α-thio-oxy-radicals undergo scission at the C–S bond to open the thia*cyclo*hexane ring and to liberate SMe groups respectively (see scheme).


Free-radical chain initiation:
RH —(−H)→ R· (1)
Chain propagation:
R· + O₂ → R·O₂· (2)
R·O₂· + RH → R·O₂H + R· (3)
Sulphoxide formation:
R·O₂H + RH → R·OH + Sulphoxide (4)
Decomp. of monothioacetal and hydroperoxide:
R·OH → H₂O + Polymers (5)
R·O₂H → HO· + R·O·
·S·[CH₂]₄·CHO → ½(I) (6)
HO· + RH → H₂O + R· (7)
(R = thiacyclohex-2-yl)

If it is assumed that two-thirds of the hydroperoxide formed in reaction (3) participates in reaction (4) and the remainder in reaction (6), the relative yields of sulphoxide, water, and disulphide (I) are 1·0 : 1·5 : 0·25, which is essentially the experimental finding, *viz.*, 1·0 : 1·3 : 0·2, with 95% of the absorbed oxygen accounted for.

The autoxidation of 2-ethyl-2-methyl-5-*iso*propylthia*cyclo*pentane (a product of the reaction of sulphur with the di-isoprenic, 2 : 6-dimethylocta-2 : 6-diene) [4] follows a pattern similar to the above. Sulphoxide, water, and a "dimeric" derivative are again the principal products, but in this case the last is not simply the analogue of (I), *i.e.*, (II),

[1] Part VII, Bateman, Cunneen, and Ford, *J.*, 1956, 3056.
[2] Bateman and Shipley, *J.*, 1955, 1996.
[3] Bateman and Hargrave, *Proc. Roy. Soc.*, 1954, *A*, **224**, 389, 399; Hargrave *ibid.*, 1956, *A*, **235**, 55.
[4] Bateman, Glazebrook, Moore, and Saville, Proc. Third Internat. Rubber Tech. Conf., London, 1954, p. 298.

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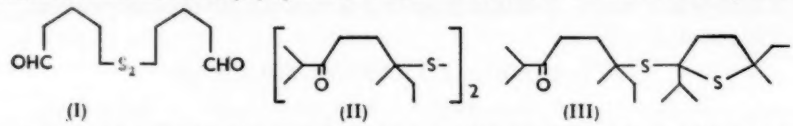
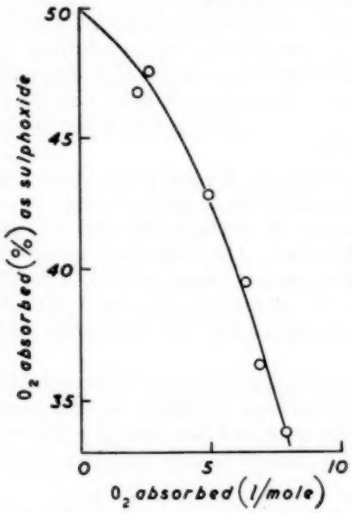
but also comprises in major amount the monoketone (III). The monoketone could be separated from the diketone (II) by vacuum-distillation, and was characterized by elemental



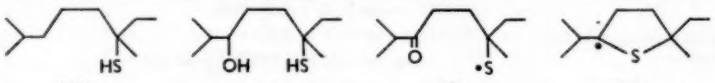
(I) (II) (III)

analysis, molecular weight, infrared absorption at 1720 cm.$^{-1}$ (associated with a saturated carbonyl group), formation of a liquid mono-2 : 4-dinitrophenylhydrazone, and reduction to the thiols (IV) and (V) and the original sulphide on treatment by lithium aluminium hydride (reflecting selective response of thioacetal-type C–S bonds to this reagent).



Variation in yield of sulphoxide during autoxidation of thiacyclohex-3-ene at 55°.

The formation of the monoketone (III) in preference to that of the diketone (II) appears indicative of favoured cross-termination of the radicals (VI) and (VII) rather than mutual combination of (VI) as in reaction (6). This is in keeping with the trend observed with highly reactive and heavily substituted olefinic systems.[5] If one adopts the reaction



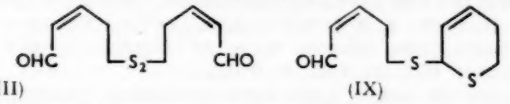
(IV) (V) (VI) (VII)

scheme given above, with one-quarter of the hydroperoxide produced as in reaction (3) participating in reaction (4) and the remainder in reaction (6), and with five out of seven radicals (VI) produced as in (6) combining with (VII), the relative yields of sulphoxide, water, and products (II) and (III) are 1·0 : 4·0 : 0·5 : 2·1 compared with the experimentally observed 1·0 : 3·3 : 0·4 : 2·4, and 82% of the absorbed oxygen is thus accounted for.

The unsaturated cyclic sulphide, thia*cyclo*hex-3-ene, readily reacted with oxygen in the absence of catalyst and, simulating further the acyclic analogues,[1] the sulphoxide was formed in approximately 50% yield (based on the oxygen absorbed) at the beginning of the reaction which fell markedly as reaction proceeded (Figure). The products consisted of thia*cyclo*hex-3-ene oxide, water, and a sulphur-containing aldehyde mixture. After separation by chromatography over silica gel, the last polymerized fairly readily at room

[5] Bateman and Morris, *Trans. Faraday Soc.*, 1953, **49**, 1026.

temperature, but if distilled rapidly in a vacuum immediately after isolation yielded a compound $C_{10}H_{14}OS_2$ identified as the monoaldehyde (IX) by its spectroscopic properties and by formation of a crystalline 2 : 4-dinitrophenylhydrazone. Treatment of the mixture



(VIII) (IX)

before distillation with Brady's reagent gave a solid heterogeneous 2 : 4-dinitrophenylhydrazone, whose analysis showed it to be derived mainly from a product containing one aldehyde group associated with each sulphur atom as well as from (IX). By this fact, the formation of the product (IX), and analogy with the oxidative fission of saturated cyclic sulphides as described above, this product is almost certainly the dialdehyde (VIII). There can be little doubt, therefore, that the autoxidation proceeds by the variant of the reaction scheme previously advanced for unsaturated sulphides, *i.e.*, by reactions identical with (1)—(4) and then the sulphoxide participates self-destructively in the subsequent decompositions.[1,3]

Experimental

Thia*cyclo*hexane, prepared from 1 : 5-dibromopentane and hydrated sodium sulphide,[6] had b. p. 140—141°/760 mm., n_D^{20} 1·5062 (Found : C, 58·8; H, 9·8; S, 31·55. Calc. for $C_5H_{10}S$: C, 58·9; H, 9·8; S, 31·4%). The derived sulphoxide had b. p. 127—128°/15 mm., n_D^{35} 1·5080 (Found : SO content, 98·0%), and the sulphone [6] had m. p. 97—98° after crystallisation from ethanol.

2-Ethyl-2-methyl-5-*iso*propylthia*cyclo*pentane [7] had b. p. 86·5°/12 mm., n_D^{20} 1·4765 (Found : C, 70·05; H, 11·4; S, 18·6. Calc. for $C_{10}H_{20}S$: C, 69·8; H, 11·6; S, 18·6%). The *sulphoxide* had b. p. 72—74°/0·01 mm., n_D^{20} 1·4892 (Found : C, 64·0; H, 10·55; S, 16·6; SO content 98·4. $C_{10}H_{20}OS$ requires C, 63·8; H, 10·6; S, 17·0%).

*Synthesis of Thia*cyclo*hex-3-ene.*—Thia*cyclo*hexan-4-ol (53 g.), m. p. 52—53°, was obtained by reduction of thia*cyclo*hexan-4-one [8] (62 g.) with lithium aluminium hydride (10 g.) in dry ether (500 ml.). Dehydration of the alcohol (40 g.) with boric acid (20 g.), first at 190° and later at 300°, gave thia*cyclo*hex-3-ene (20 g.), b. p. 71—72°/60 mm., n_D^{20} 1·5346 (Found : C, 59·85; H, 8·0; S, 32·0. Calc. for C_5H_8S : C, 60·0; H, 8·0; S, 32·0%). The derived *sulphoxide* had b. p. 71·5°/0·002 mm., n_D^{20} 1·5483 (Found : C, 51·2; H, 6·9; S, 27·1; SO content, 98·2. C_5H_8OS requires C, 51·75; H, 6·9; S, 27·6%). The sulphone had m. p. 72° (Found : C, 45·2; H, 6·1; S, 24·2. Calc. for $C_5H_8O_2S$: C, 45·4; H, 6·1; S, 24·2%).

Oxidations.—Oxidations were carried out in the apparatus described in Part VII.[1] The saturated sulphides were oxidised at 75° in the presence of αα′-azo*iso*butyronitrile (1%); thia*cyclo*hex-3-ene was oxidised at 55° without catalyst.

*Separation and Identification of the Oxidation Products of Thia*cyclo*hexane.*—The oxidised sulphide (65·37 g. containing 0·94 g. of oxygen) was heated at 50° (bath)/11 mm. and the volatile materials (59·7 g.) were collected at −80°. The infrared spectrum of the volatile product after drying (Found : C, 58·95; H, 9·75; S, 31·5%) was identical with that of the original sulphide. The involatile residue (A) (5·6 g.) had n_D^{20} 1·5040 (Found : C, 52·7; H, 8·55; N, 1·9; S, 23·0; SO content, 51%; *M*, 210); strong absorption at 1720 cm.$^{-1}$ indicated the presence of saturated carbonyl groups, and Schiff's reagent showed the presence of aldehyde groups.

A solution of the residue (A) (8·15 g.) in tetrahydrofuran was added to excess of lithium aluminium hydride in the same solvent and refluxed for 2 hr. Working up in the usual way followed by fractional distillation gave : (i) thia*cyclo*hexane (4 g.), b. p. 63—64°/50 mm., n_D^{20} 1·5052, infrared spectrum identical with that of the pure sulphide; (ii) (1·3 g.), b. p. 101°/10 mm., n_D^{20} 1·4875 (Found : C, 49·7; H, 10·0; S, 26·75; SH content, 26·25. $C_5H_{12}OS$ requires C, 50·0; H, 10·0; S, 26·66; SH content, 27·5%), identified as 5-*mercaptopentan*-1-*ol* (see below). The derivative obtained on reaction with 1-chloro-2 : 4-dinitrobenzene had m. p. and mixed m. p. 95°.

Synthesis of 5-Mercaptopentan-1-*ol.*—Reduction of but-3-enoic acid (20 g.) with lithium

[6] Whitehead, Dean, and Fidler, *J. Amer. Chem. Soc.*, 1951, **73**, 3632.
[7] Glazebrook and Saville, *J.*, 1954, 2099.
[8] Fennel and Carmack, *J. Amer. Chem. Soc.*, 1948, **70**, 1813.

aluminium hydride gave pent-4-en-1-ol (10 g.), b. p. 140—142°/760 mm., n_D^{20} 1·4295, which reacted exothermally with thioacetic acid (9 g.) to give 5-*acetylthiopentan*-1-*ol* (12 g.), n_D^{20} 1·4889 (Found: C, 52·0; H, 8·75; S, 19·6. $C_7H_{14}O_2S$ requires C, 51·9; H, 8·65; S, 19·75%). Alkaline hydrolysis of this ester gave 5-mercaptopentan-1-ol (8 g.), b. p. 104°/11 mm., n_D^{20} 1·4865 (Found: C, 49·8; H, 10·05; S, 26·4; SH content, 28·0%), which gave the 2 : 4-*dinitrophenyl sulphide*, yellow plates (from ethanol), m. p. 95° (Found: C, 46·15; H, 4·85; N, 9·8. $C_{11}H_{14}O_5N_2S$ requires C, 46·1; H, 4·82; N, 9·78%).

Reaction of Residue (A) *with* 2 : 4-*Dinitrophenylhydrazine*.—Residue (A) (4 g.) was treated with excess of 2 : 4-dinitrophenylhydrazine hydrochloride in ethanol, water added until no further precipitation occurred, and the mixture kept for 48 hr. at room temperature. The solid was filtered off, washed thoroughly with 2N-hydrochloric acid, and then with water, dried, dissolved in benzene, and poured on a column of alumina. Elution with 1 : 1 benzene–ethyl acetate, followed by evaporation, gave the 2 : 4-dinitrophenylhydrazone of the aldehydic *disulphide* (I) (1·45 g.), m. p. 122·5—124° (from benzene–*cyclo*hexane) (Found: C, 44·45; H, 4·65; N, 18·7; S, 10·75%; *M*, 640. $C_{22}H_{26}O_8N_8S_2$ requires C, 44·4; H, 4·4; N, 18·8; S, 10·8%; *M*, 594).

Separation of Residue (A) *by Counter-current Distribution*.—Residue (A) (5 g.) was partitioned between water and ether in an apparatus containing 25 cells. The water layers were saturated with salt and extracted with chloroform which on evaporation gave thia*cyclo*hexane oxide (1·2 g.), b. p. 60—62°/0·001 mm. (Found: SO content, 98·4%). Oxidation with acid permanganate gave the corresponding sulphone, m. p. and mixed m. p. 97—98°. The ether layers, on evaporation, gave an oil (1·9 g.) which rapidly polymerised to a rubber-like material.

*Oxidation of Thia*cyclo*hexane in the Presence of the Sulphoxide*.—The sulphide (9·83 g.) containing thia*cyclo*hexane oxide (0·494 g.) and αα′-azo*iso*butyronitrile (0·095 g.) was shaken in oxygen at 75° until 1·45 wt.-% had been absorbed. The sulphoxide content was then 8·3%; the calculated value on the basis that the added sulphoxide behaves as a neutral diluent having no influence on the oxidation is 8·2% (cf. *n*-butyl methyl sulphide).

Separation and Identification of the Oxidation Products of 2-*Ethyl*-2-*methyl*-5-iso*propylthia*-cyclo*pentane*.—Distillation of the oxidised sulphide (74 g. containing 1·27 g. of oxygen) at 50° (bath)/0·01 mm. gave a volatile fraction (60 g.) which contained water. After drying, infrared examination showed this fraction to be identical with the original sulphide (Found: C, 70·0; H, 11·3; S, 18·4%). The involatile residue (B) (13·83 g.) had n_D^{20} 1·5008 (Found: C, 65·7; H, 10·6; N, 0·5; S, 17·5; SO content, 10·0%). Schiff's reagent indicated the absence of aldehyde groups, but strong infrared absorption at 1720 cm.$^{-1}$ showed the presence of saturated carbonyl groups.

Residue (B) (10 g.) was partitioned between light petroleum (b. p. <40°) and water in the usual way, the water layers yielding a product which on distillation gave 2-ethyl-2-methyl-5-*iso*propylthia*cyclo*pentane oxide (1·03 g.), b. p. 73—75°/0·01 mm., n_D^{20} 1·4900 (Found: C, 64·2; H, 10·2; S, 17·1; SO content, 95·4%). The corresponding sulphone[7] had b. p. 79°/0·002 mm., n_D^{20} 1·4777. Evaporation of the light petroleum gave a mixture of ketones (C) (8·55 g.), (Found: C, 66·0; H, 10·45; N, 0·2; S, 17·55; SO content, 0·0%; *M*, 390. Calc. for 80% of $C_{20}H_{38}OS_2$ and 20% of $C_{20}H_{38}O_2S_2$: C, 66·35; H, 10·5; S, 17·7%; *M*, 350).

Mixture (C) (2·0 g.) with Brady's reagent gave a liquid derivative (2·34 g.) (Found: C, 56·6; H, 7·75; N, 11·55; S, 11·1%; *M*, 640. Calc. for 80% of $C_{26}H_{42}O_4N_4S_2$ and 20% of $C_{32}H_{46}O_8N_8S_2$: C, 56·9; H, 7·5; N, 11·4; S, 11·2%; *M*, 576). A portion of this derivative (1·1 g.) in carbon tetrachloride (200 ml.) was passed down a column (2 × 20 cm.) of alumina followed by (1) carbon tetrachloride (200 ml.) and (2) 1 : 4 carbon tetrachloride–benzene (100 ml.). When worked up, fraction (1) gave the 2 : 4-*dinitrophenylhydrazone* (0·89 g.) (Found: C, 58·15; H, 7·85; S, 11·75%; *M*, 525. $C_{26}H_{42}O_4N_4S_2$ requires C, 58·0; H, 7·8; S, 11·8%; *M*, 538) of the ketone (III), and fraction (2) gave the 2 : 4-*dinitrophenylhydrazone* (0·2 g.) (Found: C, 52·4; H, 6·25; S, 8·8. $C_{32}H_{46}O_8N_8S_2$ requires C, 52·3; H, 6·2; S, 8·7%) of the keto-disulphide (II); both products were liquids.

Reduction of the ketone (III) *with lithium aluminium hydride*. Distillation of the mixture (C) (20 g.) gave (i) a forerun (1·0 g.), b. p. >144°/0·001 mm., n_D^{20} 1·5000, and (ii) 2-*ethyl*-5-(1-*ethyl*-1 : 5-*dimethyl*-4-*oxohexylthio*)-2-*methyl*-5-iso*propylthia*cyclo*pentane* (III) (13 g.), b. p. 144—145°/0·001 mm., n_D^{20} 1·5010 (Found: C, 66·8; H, 10·4; S, 17·8%; *M*, 360. $C_{20}H_{38}OS_2$ requires C, 67·1; H, 10·6; S, 17·9%; *M*, 358); the intensity of the infrared absorption at 1720 cm.$^{-1}$ was indicative of the purity of this product.

Reduction of the ketone (III) (10 g.) with lithium aluminium hydride (3 g.) in dry tetrahydrofuran (40 ml.), and isolation of the product gave a liquid (9·2 g.), which on fractional distillation yielded: (i) a mixture of the original sulphide and 2 : 6-dimethyloctane-6-thiol (IV) (4·15 g.), b. p. 85—88°/11 mm., n_D^{20} 1·4760 (Found: C, 69·3; H, 11·75; S, 18·35; SH, 9·3%; *M*, 170. Calc. for 52% of $C_{10}H_{20}S$ and 48% of $C_{10}H_{22}S$: C, 69·25; H, 12·25; S, 18·5; SH, 9·3%; *M*, 172); infrared analysis confirmed that this mixture contained ~50% of the original sulphide; (ii) 6-*mercapto*-2 : 6-*dimethyloctan*-3-*ol* (V) (3·5 g.), b. p. 63—64°/0·002 mm., n_D^{20} 1·4790 (Found: C, 63·1; H, 11·6; S, 16·75; SH, 17·6%; *M*, 186. $C_{10}H_{22}OS$ requires C, 63·25; H, 11·6; S, 16·8; SH, 17·4%; *M*, 190).

Fraction (i) (4·0 g.) in ethanol (25 ml.) was refluxed with sodium (0·5 g.) in ethanol (25 ml.) for 10 min. After evaporation the solid residue (1·2 g.) was washed with light petroleum (b. p. <40°), and the distillate and the washings were poured into excess of water and extracted four times with light petroleum. Evaporation of the light petroleum gave the original sulphide (1·75 g.), b. p. 85—86°/11 mm., n_D^{20} 1·4760, identified by infrared examination. The solid residue (1·2 g.) was dissolved in water and acidified and then extracted with light petroleum. Distillation of the residue obtained after evaporation of the light petroleum gave 2 : 6-*dimethyloctane*-6-*thiol* (IV) (0·6 g.), b. p. 89°/10 mm., n_D^{20} 1·4760 (Found: C, 69·2; H, 12·2; S, 17·95; SH, 17·6. $C_{10}H_{22}S$ requires C, 69·0; H, 12·6; S, 18·3; SH, 18·95%).

Reduction of the ketonic mixture (C) *with lithium aluminium hydride.* The mixture (C) (7·8 g.) was treated with lithium aluminium hydride, and the product isolated in the usual way. The liquid (7·3 g.) obtained gave on distillation: (i) a mixture of the original sulphide and 2 : 6-dimethyloctane-6-thiol (IV) (2·78 g.), b. p. 85—89°/11 mm., n_D^{20} 1·4760 (Found: SH, 9·3%); (ii) 6-mercapto-2 : 6-dimethyloctan-3-ol (V) (3·0 g.), b. p. 63—64°/0·002 mm., n_D^{20} 1·4792 (Found: C, 63·95; H, 11·55; S, 17·0; SH, 16·5%; *M*, 186).

Oxidation of 2-*Ethyl*-2-*methyl*-5-iso*propylthia*-cyclo*pentane in the Presence of the Sulphoxide.*—The sulphide (8·78 g.) containing 2-ethyl-2-methyl-5-*iso*propylthia*cyclo*pentane oxide (0·211 g.) and αα′-azo*iso*butyronitrile (0·089 g.) was shaken in oxygen until 1·65 wt.-% was absorbed. The sulphoxide content was then 4·0%; the calculated value on the basis that the added sulphoxide behaves as a neutral diluent having no influence on the oxidation is 4·4%.

*Separation and Identification of the Oxidation Products of Thia*cyclo*hex-3-ene.*—The oxidised sulphide (44·31 g. containing 1·56 g. of oxygen) was distilled at 50° (bath)/11 mm.; a volatile fraction (33·6 g.) which contained water was obtained and an involatile residue (D) remained. Infrared examination of the volatile fraction after drying indicated that it was unchanged sulphide (Found: C, 59·75; H, 8·1; S, 31·95%). The residue (D) (10·5 g.) had n_D^{20} 1·5580 (Found: C, 52·6; H, 8·7; S, 27·45; SO, 50·0%; *M*, 150); infrared analysis in carbon tetrachloride indicated the presence of the following functional groups: SO (1044 cm.$^{-1}$), C:C·CO (1700 cm.$^{-1}$), C:C·S (1598 cm.$^{-1}$), and OH (3602 cm.$^{-1}$). Reaction with Schiff's reagent indicated the presence of aldehyde groups.

Residue (D) (7·3 g.) in carbon tetrachloride (200 ml.) was passed down a column (50 × 2·0 cm.) of silica gel (200-mesh) followed by (1) 3 : 1 carbon tetrachloride–ether (200 ml.), (2) ether (200 ml.), and (3) methanol (300 ml.). On working up these fractions, (1) gave a liquid (E) (3·1 g.), n_D^{20} 1·5980 (Found: C, 53·8; H, 6·85; S, 27·9; SO, 5·0%; *M*, 187), which polymerised at room temperature, with 2 : 4-dinitrophenylhydrazine in ethanol gave a heterogeneous hydrazone, m. p. 110—118° (Found C, 45·95; H, 4·4; S, 12·65%; *M*, 510. Calc. for 32% of $C_{16}H_{18}O_4N_4S_2$ and 68% of $C_{22}H_{22}O_8N_8S_2$: C, 46·0; H, 4·0; S, 12·55%; *M*, 528), and on evaporative distillation immediately after isolation gave 5-(*thia*cyclo*hex*-3-*en*-2-*ylthio*)-*pent*-2-*enal* (IX), b. p. 50°/0·001 mm., n_D^{20} 1·5954 (Found: C, 56·4; H, 6·5; S, 29·8; SO, 0%; *M*, 220. $C_{10}H_{14}OS_2$ requires C, 56·1; H, 6·5; S, 29·9%; *M*, 214), infrared bands at 1700 (C:C·CO) and 1598 cm.$^{-1}$ (C:C·S), which with Brady's reagent gave the dark red 2 : 4-*dinitrophenylhydrazone*, m. p. 122° (from 1 : 1 benzene–*cyclo*hexane) (Found: C, 48·9; H, 4·6; N, 14·35%; *M*, 425. $C_{16}H_{18}O_4N_4S_2$ requires C, 48·7; H, 4·6; N, 14·2%; *M*, 394) [light absorption max. in EtOH at 3740 Å (ε 29,700)], of (IX). Fraction (2) gave only a trace of extract, but fraction (3) gave a product (3·5 g.) which on distillation yielded thia*cyclo*hex-3-ene oxide, b. p. 71—73°/0·002 mm., n_D^{20} 1·5480 (sulphone, m. p. and mixed m. p. 72°).

Residue (D) (3·0 g.) with lithium aluminium hydride in tetrahydrofuran gave thia*cyclo*hex-3-ene (1·75 g.), b. p. 70—72°/60 mm., n_D^{20} 1·5340, and a residue (0·85 g.), which contained thiol groups (lead acetate).

Quantitative Estimation of Oxidation Products.—Sulphoxide and water. These were estimated

by the procedures described in Part VII. With the saturated sulphides, there was little variation in yields during the reaction. Results are tabulated.

O_2 absorbed	Thia*cyclo*hexane				2-Ethyl-2-methyl-5-*iso*propyl-thia*cyclo*pentane		
Wt. %	0·30	0·56	0·92	1·64	0·30	0·95	1·93
Found as sulphoxide (%)	38	35	36	32	14	11	8
Found as water (%)	—	—	48	46	37	36	35

Aldehydic disulphide (I). This was estimated in three ways: (i) from the amount of 5-mercaptopentan-1-ol isolated from the reduction of residue (A) with lithium aluminium hydride; (ii) gravimetrically, from the chromatographically purified 2 : 4-dinitrophenylhydrazone obtained by reaction of residue (A) with Brady's reagent; and (iii) polarographically from the polarogram of residue (A) in 85 : 15 (v/v) acetone-free methanol–water containing 0·025M-tetramethylammonium bromide at a dropping-mercury cathode, the diffusion coefficient of these disulphide groups being assumed equal to that of *n*-butyl disulphide. The three methods gave values of 15·6, 14·3, and 18·0%, respectively, for the amount of (I) present in (A), and the mean value of 16% was used for the calculations in the Table below.

Oxo-disulphide (II) *and ketone* (III). These were estimated gravimetrically after chromatographic separation of the 2 : 4-dinitrophenylhydrazones obtained by reaction of residue (C) with Brady's reagent.

From these estimations the approximate distribution of the absorbed oxygen is as expressed below for thia*cyclo*hexane at an uptake of 1·43 wt.-% of oxygen and for 2-ethyl-2-methyl-5-*iso*propylthia*cyclo*pentane at an uptake of 1·71 wt.-% of oxygen.

	Thia*cyclo*hexane			2-Ethyl-2-methyl-5-*iso*propylthia-*cyclo*pentane			
	H_2O	Sulphoxide	(I)	H_2O	Sulphoxide	(II)	(III)
O_2 absorbed (%)	47	35	13	36	11	9	26

Thiol groups. The thiol (0·1 milliequiv.) in 95% ethanol (100 ml.) was titrated with 0·00931N-silver nitrate, the end-point being determined amperometrically with a spinning platinum electrode and a calomel cell.[9]

We are indebted to Mr. G. Higgins for the spectroscopic data.

British Rubber Producers' Research Association,
48–52 Tewin Road, Welwyn Garden City, Herts. [*Received, November 5th*, 1956.]

[9] Kolthoff and Harris, *Ind. Eng. Chem. Analyt.*, 1946, **18**, 161.

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296. *Nitro-compounds as Amœbicides. Part I. Compounds related to 2-Di-(2-hydroxyethyl)amino-5-nitropyridine.*

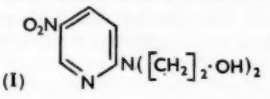
By A. R. Brown, F. C. Copp, and A. R. Elphick.

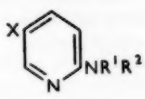
The discovery [1] that 2-di-(2-hydroxyethyl)amino-5-nitropyridine [2] is amœbicidal prompted the preparation of a number of related compounds by known methods. With certain exceptions, Mangini's method was suitable for reaction of 2-chloro-5-nitropyridine and the appropriate bases, including esters of amino-acids.

During routine screening of different compounds for chemotherapeutic activity it was observed [1] that 2-di-(2-hydroxyethyl)amino-5-nitropyridine [2,3] (I) had amœbicidal properties (*Entamoeba histolytica*) when tested in rats. Soon after this the antihistomonas (*Histomonas meleagridis*) properties of 2-amino-5-nitro-thiazole and -pyrimidine were

[1] Neal and Vincent, *Brit. J. Pharmacol.*, 1955, **10**, 434.
[2] Copp and Timmis, *J.*, 1955, 2021.
[3] B.P. 700,757.

announced [4] and further tests in our own laboratories [5] showed that both these two compounds and 2-amino-5-nitropyridine were also amœbicides. Many compounds, known and new, have since been prepared and tested and the compounds more closely related to the active compound (I) are here reported.


(I)


(II)

Most of the compounds containing the 5-nitro-group were obtained by condensing the appropriate amine and 2-chloro-5-nitropyridine in alcoholic sodium acetate [6] though the ease of reaction was much affected by steric factors. Thus, di-(2-hydroxyethyl)amine and 2-chloro-5-nitropyridine were shown [2] to react quite quickly under these conditions but 2-hydroxyethyl-2-hydroxypropylamine reacted with 2-bromo-5-nitropyridine only at 130° and in the absence of a diluent, whilst di-(2-hydroxypropyl)amine did not react with 2-chloro- or 2-bromo-5-nitropyridine without gross decomposition. 2-Bromo-5-chloro- and 2 : 5-dibromo- but not 2-bromo-5-iodo-pyridine gave the desired products (II; $R^1 = R^2 = [CH_2]_2{\cdot}OH$, X = Cl and Br respectively) when treated with neat diethanolamine at 180°. The iodo-compound (II; $R^1 = R^2 = [CH_2]_2{\cdot}OH$, X = I) was therefore prepared by iodination of the amine (II; $R^1 = R^2 = [CH_2]_2{\cdot}OH$, X = H) in the presence of mercuric acetate. It has been shown that under these conditions 2-aminopyridine gives 2-amino-5-iodopyridine.[7] Reduction of the compound (I) with cold stannous chloride gave the corresponding amine (II; $R^1 = R^2 = [CH_2]_2{\cdot}OH$, $X = NH_2$).

Although it has since been shown that the di-(2-hydroxyethyl)amine (I) has a direct inhibitory action upon amœba,[1] it originally seemed possible that the effective chemotherapeutic agent was not the di-(2-hydroxyethyl)amine *per se*, but a metabolite such as the acid (II; $R^1 = R^2 = CH_2{\cdot}CO_2H$, $X = NO_2$) which might conceivably act as an amino-acid antagonist. Unfortunately di(methoxycarbonylmethyl)amine could not be caused to react with 2-chloro- or 2-bromo-5-nitropyridine. In model experiments the ethyl esters of glycine, alanine, and sarcosine reacted readily with 2-chloro-5-nitropyridine under our usual conditions to give (II; $R^1 = H$, $R^2 = CH_2{\cdot}CO_2Et$; $R^1 = H$, $R^2 = CHMe{\cdot}CO_2Et$; and $R^1 = Me$, $R^2 = CH_2{\cdot}CO_2Et$, $X = NO_2$). The first two of these esters gave the corresponding acids on acid, but not alkaline, hydrolysis though the latter method easily gave the third parent acid. The corresponding amides and hydrazides were also prepared (except II; $R^1 = H$, $R^2 = CHMe{\cdot}CO{\cdot}NH_2$, $X = NO_2$, which was not investigated). Gruber [8] has since stated that glycine ethyl ester reacts with 2-fluoro- but not with 2-chloro-5-nitropyridine. This was probably due to the use of mildly alkaline conditions whereas we used more acid conditions (cf. Banks [9]).

Biological tests [5] have shown that of these compounds (and the related nitropyridines reported previously [2]), only (I), (II; $R^1 = [CH_2]_2{\cdot}OH$, $R^2 = CH_2{\cdot}CHMe{\cdot}OH$, $X = NO_2$), and the sarcosine derivatives (II; $R^1 = Me$, $R^2 = CH_2{\cdot}CO{\cdot}NH_2$ and $CH_2{\cdot}CO{\cdot}NH{\cdot}NH_2$, $X = NO_2$) have amœbicidal activity. The chloro-derivative (II; $R^1 = R^2 = [CH_2]_2{\cdot}OH$, X = Cl) appeared to be active in the original tests but these could not be confirmed (cf. ref. 3).

Experimental

2-Hydroxyethyl-3-hydroxypropylamine.—3-Hydroxypropylamine (39 g.) and ethylene oxide (20 ml.) were heated in ethanol (80 ml.) in an autoclave at 100° for 1 hr. The ethanol was then

[4] Waletzky, Clark, and Marson, *Science*, 1950, **111**, 720.
[5] Personal communication from Dr. Neal and Miss Vincent.
[6] Mangini and Frenguelli, *Gazzetta*, 1939, **69**, 86.
[7] Shepherd and Fellows, *J. Amer. Chem. Soc.*, 1948, **70**, 157.
[8] Gruber, *Canad. J. Chem.*, 1953, **31**, 1020.
[9] Banks, *J. Amer. Chem. Soc.*, 1944, **66**, 1127.

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evaporated and the residue distilled *in vacuo*. The *product* (35 g.) was a viscous liquid, b. p. 160—162°/11 mm. (Found: C, 51·0; H, 10·8. $C_5H_{13}O_2N$ requires C, 50·4; H, 11·0%).

2-(2-*Hydroxyethyl*-2-*hydroxypropylamino*)-5-*nitropyridine and Related Nitropyridines.*—2-Hydroxyethyl-2-hydroxypropylamine [10] (10 g.) and 2-bromo-5-nitropyridine (8 g.) were heated at 130° for 3 hr. The cooled mixture was poured into excess of 2N-hydrochloric acid, the insoluble portion filtered off, and the parent base precipitated with potassium carbonate and then extracted with ethyl acetate. This base was a gum but its *hydrochloride* crystallised without difficulty (see Table).

Derivatives of 5-nitropyridine.

Substituent(s)	No.	Deriv.	M. p.	Solvent for crystn.
2-N<[CH$_2$]$_2$·OH, CH$_2$·CHMe·OH	1	HCl	131°	EtOH–EtOAc
2-NEt·[CH$_2$]$_2$·OH	2	HCl	147—148	EtOH
2-NPr·[CH$_2$]$_2$·OH	3	HCl	153—154	EtOH
2-N<[CH$_2$]$_2$·OH	4	Base	68—69	—
[CH$_2$]$_2$·OH	5	HCl	123—124	EtOH–EtOAc
2-N([CH$_2$]$_2$·OH)$_2$	6	Base	43—45	—
2-N([CH$_2$]$_2$·OH)$_2$; 3-Me	7	HCl	157	EtOH
2-N([CH$_2$]$_2$·OH)$_2$; 4-Me	8	HCl	138—139	EtOH–EtOAc
2-N([CH$_2$]$_2$·OH)$_2$; 6-Me	9	Base	108—109	EtOH

	Found (%)					Required (%)			
No.	C	H	N	Cl	Formula	C	H	N	Cl
1	43·3	5·5	—	—	$C_{10}H_{15}O_4N_3$,HCl	43·3	5·8	—	—
2	—	—	—	14·2	$C_9H_{13}O_3N_3$,HCl	—	—	—	14·3
3	—	—	—	14·0	$C_{10}H_{15}O_3N_3$,HCl	—	—	—	13·6
4	50·1	6·1	17·2	—	$C_{10}H_{15}O_4N_3$	49·8	6·3	17·4	—
5	—	—	—	12·9	$C_{10}H_{15}O_4N_3$,HCl	—	—	—	12·7
6	51·9	6·25	16·8	—	$C_{11}H_{17}O_4N_3$	51·75	6·7	16·5	—
7	43·2	5·8	14·7	—	$C_{10}H_{15}O_4N_3$,HCl	43·3	5·8	15·1	—
8	43·3	5·8	—	—	$C_{10}H_{15}O_4N_3$,HCl	43·3	5·8	—	—
9	49·7	6·1	17·0	—	$C_{10}H_{15}O_4N_3$	49·8	6·3	17·4	—

The more closely related nitropyridines are described in the Table. They were prepared from 2-chloro-5-nitropyridine and the appropriate base according to the previously used method.[5, 6] 2-(Ethyl-2-hydroxyethylamino)-5-nitropyridine has already been prepared.[11] Apart from the hydrochlorides, the nitropyridines described in this paper were bright yellow.

2-*Amino*-5-*chloro-* *and* 2-*Amino*-5-*bromo-pyridine.*—The first of these compounds was prepared by chlorination of 2-aminopyridine in 20% sulphuric acid as previously described [12] but the crude product was more easily purified by steam-distillation, almost pure 2-amino-5-chloropyridine being thus obtained; it was converted directly into 2-bromo-5-chloropyridine by established methods.[13, 14]

2-Amino-5-bromopyridine was similarly prepared but the product from steam-distillation was a mixture. This was dissolved in a slight excess of hot 2N-acetic acid. On cooling, the feebly basic 2-amino-3:5-dibromopyridine crystallised. This was filtered off and the filtrate basified to give 2-amino-5-bromopyridine, m. p. 136—137° (49%), which was then converted into 2:5-dibromopyridine.[13–15]

5-*Chloro-* *and* 5-*Bromo*-2-*di*-(2-*hydroxyethyl*)*aminopyridine.*—2-Bromo-5-chloropyridine (20 g.) and diethanolamine (24 g.) were warmed in a Carius tube to 100°. The mixture was well shaken at this temperature, an essential precaution, and then heated to 170° for 8 hr. After cooling, the crude mixture was poured into excess of 4N-ammonia and repeatedly extracted with ethyl acetate. The combined extracts were dried (K_2CO_3) and evaporated. The residue was converted into its *hydrochloride*, which was crystallised once from ethanol and ether and then from propan-2-ol, m. p. 143° (12·1 g.) (Found: C, 42·8; H, 5·7; N, 10·7; Cl, 28·1. $C_9H_{13}O_2N_2Cl$,HCl requires C, 42·7; H, 5·6; N, 11·1; Cl, 28·1%). The parent *base* was extracted

[10] Cottle, Jeltsch, Stoudt, and Walter, *J. Org. Chem.*, 1946, **11**, 286.
[11] Bremer, *Annalen*, 1936, **521**, 286.
[12] English, Clark, Clapp, Seeger, and Ebel, *J. Amer. Chem. Soc.*, 1946, **68**, 458.
[13] Craig, *ibid.*, 1934, **56**, 231.
[14] Case, *ibid.*, 1946, **68**, 2574.
[15] Leese and Rydon, *J.*, 1954, 4039.

from a basified solution of the above hydrochloride with chloroform. It slowly solidified and had m. p. 23—25° (Found : C, 49·8; H, 5·9; N, 12·6. $C_9H_{13}O_2N_2Cl$ requires C, 49·9; H, 6·0; N, 12·9%).

2 : 5-Dibromopyridine (6 g.) was similarly treated with diethanolamine (6 g.) for 6 hr. at 170°. The product was isolated in the same way and characterised as its *hydrochloride* (2·6 g.), m. p. 145—146° (Found : C, 36·5; H, 4·4; N, 9·7. $C_9H_{13}O_2N_2Br,HCl$ requires C, 36·3; H, 4·7; N, 9·4%). The base did not crystallise.

2-*Di*-(2-*hydroxyethyl*)*amino*-5-*iodopyridine*.—A solution of 2-di-(2-hydroxyethyl)aminopyridine [2, 16] (5·3 g.) in water (25 ml.) was treated with mercuric acetate (4·0 g.). The mixture was heated for 2 min. on a steam-bath, then cooled to 70°, and a solution of iodine (6·8 g.) in hot dioxan (30 ml.) was rapidly added. The iodine colour disappeared and precipitation occurred. The suspension was then stirred at 70° for 45 min. during which the original precipitate dissolved and a little red solid separated. After cooling to 0°, the insoluble portion was filtered off but it gave no identifiable products. The filtrate was evaporated *in vacuo* until an oil appeared. After addition of potassium iodide (10 g.), this mixture was extracted several times with ethyl acetate. The combined extracts were dried and evaporated. The residue was purified as its *hydrochloride* (5·1 g.), m. p. 116—117°, from ethanol–propan-2-ol (Found : N, 8·0; Cl^-, 10·2; I, 36·6; O, 9·7. $C_9H_{13}O_2N_2I,HCl$ requires N, 8·1; Cl, 10·3; I, 36·8; O, 9·3%). The regenerated *base*, crystallised from benzene, had m. p. 72—73° (Found : I, 41·0. $C_9H_{13}O_2N_2I$ requires I, 41·2%).

5-*Amino*-2-*di*-(2-*hydroxyethyl*)*aminopyridine*.—2-Di-(2-hydroxyethyl)amino-5-nitropyridine (9·2 g.) was reduced in 2N-hydrochloric acid (200 ml.) with stannous chloride (28·0 g.) at 15—20° in nitrogen. After removal of the tin with hydrogen sulphide, the filtrate was evaporated immediately *in vacuo*. The residual *dihydrochloride* solidified when ground with propan-2-ol and recrystallised from methanol on addition of propan-2-ol as colourless needles (6·8 g.), m. p. 178—179·5°, which darkened very rapidly in air (Found : C, 40·2; H, 6·3. $C_9H_{15}O_2N_3,2HCl$ requires C, 40·3; H, 6·3%).

N-(5-*Nitro*-2-*pyridyl*)*amino-acid Esters*.—Glycine ethyl ester hydrochloride (16·8 g.), 2-chloro-5-nitropyridine (19·2 g.), and anhydrous sodium acetate reacted in boiling ethanol (100 ml.) during 3 hr. Addition of water gave a solid precipitate which was heated at 100° *in vacuo* to remove unchanged 2-chloro-5-nitropyridine. The residual *N*-(5-nitro-2-pyridyl)glycine ethyl ester crystallised from ethanol as yellow needles, m. p. 138—139° (10·3 g.) (Found : C, 48·0; H, 4·7. Calc. for $C_9H_{11}O_4N_3$: C, 48·0; H, 4·9%). {Gruber [8] obtained this substance as " white needles," m. p. 142—143°.) Similar preparations gave N-(5-*nitro*-2-*pyridyl*)*alanine ethyl ester*, m. p. 115—116° (Found : C, 50·5; H, 5·4. $C_{10}H_{13}O_4N_3$ requires C, 50·2; H, 5·5%), and N-(5-*nitro*-2-*pyridyl*)*sarcosine ethyl ester*, m. p. 78—79° (from ethanol) (Found : C, 50·4; H, 5·2; N, 17·5. $C_{10}H_{13}O_4N_3$ requires C, 50·2; H, 5·5; N, 17·55%).

N-(5-*Nitro*-2-*pyridyl*)*amino-acids*.—A solution of *N*-(5-nitro-2-pyridyl)glycine ethyl ester (2·25 g.) in 4N-hydrochloric acid (12·5 ml.) was heated under reflux for 1 hr. and its pH then adjusted to 4—5 by ammonia. The precipitate was filtered off and recrystallised from hot water, to give N-(5-*nitro*-2-*pyridyl*)*glycine hydrate* (1·6 g.), m. p. 205° (decomp.) (Found : C, 39·4; H, 4·1; loss at 100° *in vacuo*, 8·5. $C_7H_7O_4N_3,H_2O$ requires C, 39·1; H, 4·2; H_2O, 8·4%). Its *copper salt* was precipitated from aqueous solution as green needles, decomp. 193—196° (Found : Cu, 14·2. $C_{14}H_{12}O_8N_6Cu$ requires Cu, 13·9%). N-(5-*Nitro*-2-*pyridyl*)-*alanine*, similarly prepared, had m. p. 175° (from methanol) (Found : C, 46·0; H, 4·4. $C_8H_9O_4N_3$ requires C, 45·5; H, 4·3%).

N-(5-Nitro-2-pyridyl)sarcosine ethyl ester (2·0 g.) was hydrolysed with potassium hydroxide (0·5 g.) in boiling methanol for 1 hr. The potassium salt which separated was filtered off and the parent N-(5-*nitro*-2-*pyridyl*)*sarcosine* crystallised from 10% aqueous alcohol; it had m. p. 146° (decomp.) (Found : C, 45·7; H, 3·9; N, 20·1. $C_8H_9O_4N_3$ requires C, 45·5; H, 4·3; N, 19·9%). Its *copper salt* was obtained as green needles (from water), m. p. 194—195° (Found : Cu, 12·9. $C_{16}H_{16}O_8N_6Cu$ requires Cu, 13·2%).

Amides.—A suspension of *N*-(5-nitro-2-pyridyl)glycine ethyl ester (7·7 g.) in saturated methanolic ammonia (70 ml.) was stirred at 40° for 8 hr. in an autoclave. After evaporation the residual N-(5-*nitro*-2-*pyridyl*)*glycine amide* crystallised from hot water and had m. p. 213° (2·15 g.) (Found : C, 43·2; H, 4·2; N, 28·5; O, 24·8. $C_7H_8O_3N_4$ requires C, 42·9; H, 4·1; N, 28·55; O, 24·5%). N-(5-*Nitro*-2-*pyridyl*)*sarcosine amide*, similarly prepared, had m. p.

[16] Weiner and Kaye, *J. Org. Chem.*, 1949, **14**, 868.

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158° (from methanol) (Found: C, 46·1; H, 4·7; N, 25·7. $C_8H_{10}O_3N_4$ requires C, 45·7; H, 4·8; N, 26·7%).

Hydrazides.—*N*-(5-Nitro-2-pyridyl)glycine ethyl ester (8 g.) was treated with a boiling solution of hydrazine hydrate (3·5 g.) in ethanol (30 ml.) for 4 hr. The N-(*5-nitro-2-pyridyl*)-*glycine hydrazide* which separated recrystallised from boiling water, having m. p. 212° (5·1 g.) (Found: C, 40·2; H, 4·2; N, 32·9. $C_7H_9O_3N_5$ requires C, 39·8; H, 4·3; N, 33·2%). Similar preparations gave N-(*5-nitro-2-pyridyl*)*alanine hydrazide*, m. p. 200° (from methanol) (Found: C, 42·6; H, 5·0; N, 30·4; O, 21·65. $C_8H_{11}O_3N_5$ requires C, 42·7; H, 4·9; N, 31·1; O, 21·3%), and N-(*5-nitro-2-pyridyl*)*sarcosine hydrazide*, m. p. 175° (from ethanol) (Found: C, 42·4; H, 4·8; N, 30·6; O, 21·15. $C_8H_{11}O_3N_5$ requires C, 42·7; H, 4·9; N, 31·1; O, 21·3%).

We are indebted to Mr. P. R. W. Baker of this Division for the microanalyses and to Dr. R. A. Neal and Miss P. Vincent of the Wellcome Laboratories of Tropical Medicine for the biological results.

THE WELLCOME RESEARCH LABORATORIES,
BECKENHAM, KENT. [*Received, November 27th*, 1956.]

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297. *Quantitative Aspects of the Base-catalysed Halogenation of Aliphatic Ketones. Part II.*[1] *Iodination of Non-methyl Ketones.*

By C. F. CULLIS and M. H. HASHMI.

Base-catalysed iodination of three aliphatic non-methyl ketones has been studied. The factors controlling the extent of iodine consumption are similar to those found with methyl ketones, though more stringent conditions must be satisfied to achieve the maximum halogen uptake.

Analysis of products shows that, in contrast to the behaviour of methyl ketones, the halogen effects considerable oxidation, and only a small proportion of the consumed iodine is converted into organic form.

METHYL ketones react rapidly with iodine in alkaline solution to give iodoform as the main product. Non-methyl ketones are also readily iodinated and the uptake of iodine is sometimes higher than with methyl ketones, although comparatively little iodoform is produced. An earlier study of some quantitative aspects of the base-catalysed iodination of methyl ketones [1] has now been extended to some non-methyl compounds.

EXPERIMENTAL

Purified commercial samples of diethyl ketone and di*iso*propyl ketone were used. A specimen of pure *n*-butyl ethyl ketone was kindly supplied by Dr. H. M. E. Cardwell. All ketone solutions were prepared by weight.[2]

The experimental methods were similar to those used with methyl ketones.[1]

RESULTS

Kinetic Measurements.—As with methyl ketones, a plot of $\log_{10}(T_t - T_\infty)$ against t (where T_t and T_∞ are the thiosulphate titres after times t and infinity respectively) gives a straight line,

TABLE 1. *Rates of iodination of some non-methyl ketones.*

Temp. = 25°; [Ketone] = 0·0025M; [Iodine] = 0·01M; [NaOH] = 0·1M.

Ketone	Vel. const. k (sec.$^{-1}$ × 10^3)	Ketone	Vel. const. k (sec.$^{-1}$ × 10^3)
Diethyl ketone	3·31	Di*iso*propyl ketone	2·30
n-Butyl ethyl ketone ...	3·64	(Acetone)	(16·80)

indicating that the reaction obeys an overall first-order kinetic law. The velocity constants shown in Table 1 are calculated from results in the range 0—50% of completed reaction. Comparison with the corresponding values for methyl ketones [1] shows that the non-methyl ketones are generally much less reactive.

[1] Part I, Cullis and Hashmi, *J.*, 1956, 2512.
[2] Goodwin, *J. Amer. Chem. Soc.*, 1920, **42**, 39.

With all three ketones, the rate of iodination is independent of iodine concentration, indicating that the rate-determining step involves ketone and alkali only. The relationship between rate and alkali concentration is of the form: rate $= k_0 + k_{OH^-}[OH^-]$, where k_0

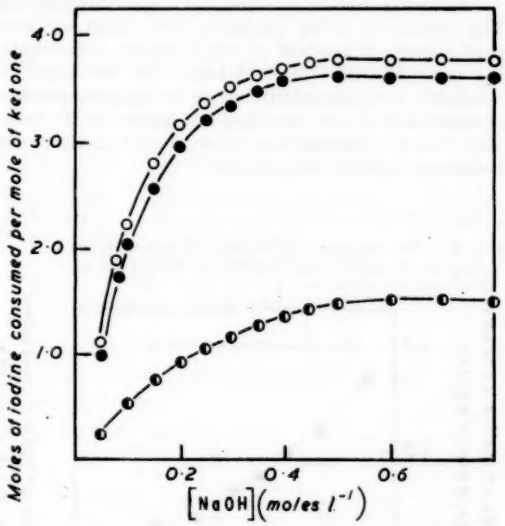


FIG. 1. *The influence of alkali concentration on iodine consumption by non-methyl ketones.*

Temp. = 25°. [Ketone] = 0·0025M. [Iodine] = 0·01M.

○, Et_2CO (3·77). ●, Et·CO·Bu^n (3·60). ◐, Pr^i_2CO (1·52).

(The figures against each ketone represent the number of moles of iodine consumed per mole of ketone when excess of alkali is present.)

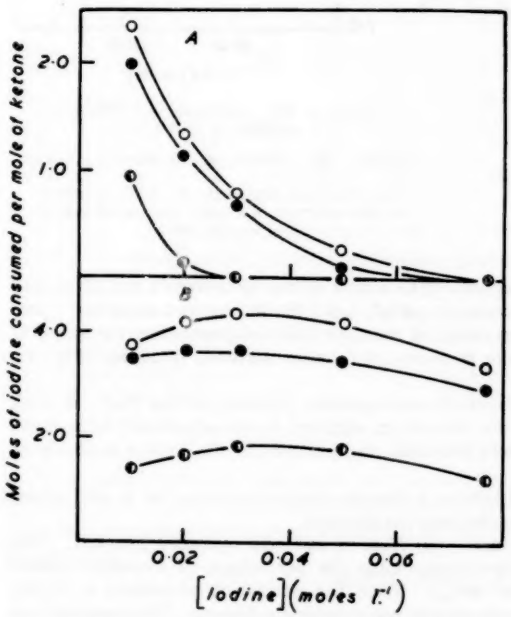


FIG. 2. *The influence of iodine concentration on iodine consumption by non-methyl ketones.*

Temp. = 25°. [Ketone] = 0·0025M.

A, [NaOH] = 0·1M. *B*, [NaOH] = 0·4M. ○, Et_2CO. ●, Et·CO·Bu^n. ◐, Pr^i_2CO.

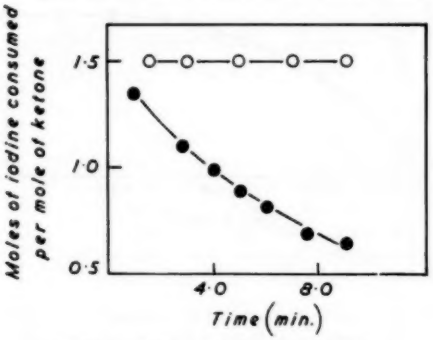
presumably represents the "spontaneous" (solvent-catalysed) rate of iodination. Thus for diethyl ketone:

$$k\ (\text{sec.}^{-1}) = 1{\cdot}90 \times 10^{-3} + 1{\cdot}52 \times 10^{-2}[OH^-]$$

The rate of exchange of deuterium with heavy water is much greater for diethyl ketone than for acetone.[3] The water-catalysed enolisation process [negligible with acetone where k_{OH^-} is large ($16{\cdot}8 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$)] therefore becomes significant with diethyl ketone for which k_{OH^-} is much smaller.

Factors controlling the Extent of Iodine Consumption.—(a) *Influence of reagent concentrations.* The uptake of iodine increases with alkali concentration (Fig. 1), but the limiting iodine consumption is reached at much higher concentrations ([NaOH] $\geqslant$ 0·5M) than with methyl ketones ([NaOH] = 0·08—0·15M). At low alkali concentrations, excess of iodine has a markedly unfavourable influence on halogen uptake [Fig. 2(*A*)]; at a higher pH, the iodine consumption at first increases but subsequently falls again [Fig. 2(*B*)]. Separate experiments show that the decrease may be attributed partly to a lowering of pH and partly to an increase in potassium iodide concentration.

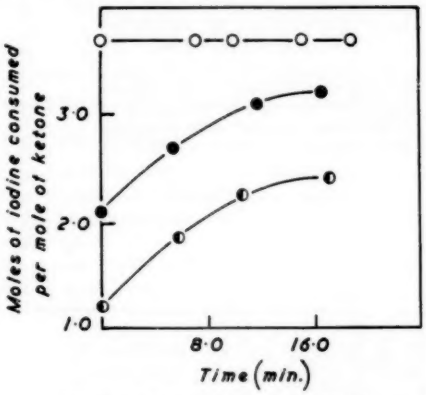
FIG. 3. *The influence of the order of mixing of the reagents on iodine consumption by diethyl ketone.*



Temp. = 25°. [Ketone] = 0·0025M. [Iodine] = 0·01M. [NaOH] = 0·05M.

○ Ketone and sodium hydroxide mixed, iodine added after time *t*.
● Iodine and sodium hydroxide mixed, ketone added after time *t*.

FIG. 4. *The influence of the rate of addition of iodine on iodine consumption by diethyl ketone.*



Temp. = 25°. [Ketone] = 0·0025M. [Iodine] = 0·01M.

[NaOH]: ◑ = 0·05M; ● = 0·1M; ○ = 0·4M.

[The abscissæ represent the time, *t*, taken for the addition of a fixed volume of iodine solution (25 ml.).]

(b) *Order and rate of addition of the reagents.* The iodine uptake decreases if the alkali and iodine are mixed and set aside before the ketone is added, but if the ketone and alkali are "premixed" the consumption of iodine is independent of the time which elapses before the iodine is run in (Fig. 3). The total halogen uptake is increased by slow addition of iodine (Fig. 4), particularly at low alkali concentrations.

Identification of reaction products. Paper-chromatographic analysis shows that, as with methyl ketones, iodinated organic acids are formed in addition to unsubstituted fatty acids (Table 2). The nature of the acid products indicates the positions in the ketone molecule at which C–C bond cleavage takes place.

With diethyl ketone and *n*-butyl ethyl ketone, yellow crystals of iodoform, m. p. and mixed m. p. 119° (lit., m. p. 119°), separated from the reaction mixture.

Quantitative Analysis of Reaction Products.—(a) *Neutral and acid iodinated products.* The results in Table 3 show that with all three compounds the percentage of consumed iodine extracted is remarkably low (usually 20—40%). Since the extraction procedure is highly efficient (>98%),[1] all the iodine taken up is clearly not organically-bound. This implies that most of the consumed halogen is used for oxidation purposes according to the process $I_2 + 2e = 2I^-$, and is thereby converted into inorganic form. With diethyl ketone and *n*-butyl ethyl

[3] Gordon and McNesby, unpublished results.

ketone, the major part of the organically bound iodine is present in neutral form, while with di*iso*propyl ketone the iodinated products consist mainly of iodo-acids [α-iodo*iso*butyric acid (α-iodo-α-methylpropionic acid)].

(b) *Iodoform.* Analysis shows that all the iodine in neutral organic form is present as iodoform, though with di*iso*propyl ketone the quantity formed is very small (Table 4).

TABLE 2. *Acids formed in the base-catalysed iodination of some non-methyl ketones.**

Temp. = 25°; [Ketone] = 0·0025M; [Iodine] = 0·01M; [NaOH] = 0·4M.

Ketone	Acids formed: Fatty acids	Acids formed: Iodo-acids
Et|CO·Et	$Me·CO_2H$, 0·38 (0·39) $Et·CO_2H$, 0·47 (0·48)	$Me·CHI·CO_2H$, 0·55 (0·55)
Et|CO|Bu^n	$Me·CO_2H$, 0·38 (0·39) $Et·CO_2H$, 0·47 (0·48) $Bu^n·CO_2H$, 0·68 (0·68)	$Me·CHI·CO_2H$, 0·55 (0·55) $Pr^n·CHI·CO_2H$, 0·71 (0·72 for isomeric $Pr^i·CHI·CO_2H$)
Pr^i|CO·Pr^i	None	$Me_2CI·CO_2H$, 0·64 (0·65)

* R_F values of acids present in products are given together with the corresponding values determined for the known acids in parentheses. The developing solvent contained 30% v/v aqueous ammonia (*s.g.* 0·88) and 70% v/v *n*-propyl alcohol.

TABLE 3. *Influence of iodine concentration on the iodinated products formed from non-methyl ketones.*

Temp. = 25°; [Ketone] = 0·0025M; [NaOH] = 0·5M.

[Iodine] (mole l.$^{-1}$)	Moles of iodine per mole of ketone: Found: Neutral	Acid	Total	Consumed	Extraction (%)
Diethyl ketone					
0·0075	0·18	0·05	0·23	3·00	8·1
0·01	0·53	0·07	0·60	3·82	15·9
0·03	0·87	0·12	0·89	4·54	21·6
0·075	0·70	0·10	0·80	3·55	22·4
n-Butyl ethyl ketone					
0·0075	0·80	0·20	1·00	3·00	33·7
0·01	0·75	0·33	1·08	3·60	30·1
0·03	0·86	0·30	1·16	3·68	31·8
0·075	0·85	0·34	1·19	3·02	39·5
Di*iso*propyl ketone					
0·0075	0·06	0·36	0·42	1·46	29·3
0·01	0·06	0·36	0·42	1·46	29·3
0·03	0·12	0·58	0·70	1·84	38·0
0·075	0·06	0·38	0·44	1·24	36·8
Diacetyl					
0·01	—	—	1·07	2·66	40·5

TABLE 4. *Iodoform present in the neutral iodinated products.*

Temp. = 25°; [Ketone] = 0·0025M; [Iodine] = 0·01M; [NaOH] = 0·5M.

Ketone	Moles of iodine per mole of ketone: Neutral organic form (found by total halogen analysis)	Iodoform (found by spectroscopic absorption)
Diethyl ketone	0·53	0·48
n-Butyl ethyl ketone	0·75	0·71
Di*iso*propyl ketone	0·06	0·05

DISCUSSION

The base-catalysed iodination of methyl ketones proceeds mainly according to equation (1). The corresponding reaction for non-methyl ketones follows a somewhat different course and is rarely accompanied by the production of more than small quantities of iodoform.

$$R·COMe + 3I_2 + 4NaOH = CHI_3 + R·CO_2Na + 3NaI + 3H_2O \quad . \quad . \quad . \quad . \quad (1)$$

The factors controlling iodine uptake are similar to those operative with methyl ketones, though comparison shows that with non-methyl compounds much more stringent conditions are required to achieve the limiting uptake of halogen. Since the extent of iodine consumption depends on a balance between the rates of halogenation of the ketone

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and of disproportionation of hypoiodite to iodate, the necessity of retarding the latter process should be greater with the comparatively unreactive non-methyl ketones. Thus the favourable effect of alkali concentration (Fig. 1), the unfavourable influence of excess of iodine (Fig. 2), and the need for slow addition of the iodine to the pre-mixed ketone–alkali solution (Fig. 4) are even more in evidence with non-methyl ketones as factors controlling the halogen consumption.

The base-catalysed iodination of non-methyl ketones is mechanistically more complex than the corresponding process for methyl ketones. A marked difference is provided by the analytical results, which show that with non-methyl ketones only a small percentage of the consumed iodine is converted into organic form.

Levine and Stephens [4] studied the reaction of propiophenone with sodium hypobromite. Successive bromination at the CH_2 group yields 2:2-dibromopropiophenone, which is then hydrolysed to 1-phenylpropane-1 : 2-dione. The latter in presence of sodium hypobromite suffers oxidative fission across the CO–CO bond to give a high yield (>90%) of benzoic and acetic acids. The main overall reaction is thus :

$$Ph{\cdot}CO{\cdot}CH_2{\cdot}CH_3 + 3Br_2 + 8NaOH = Ph{\cdot}CO_2Na + Me{\cdot}CO_2Na + 6NaBr + 5H_2O \quad . \quad (2)$$

and all the consumed halogen reappears in inorganic form. An analogous reaction with aliphatic non-methyl ketones may be responsible for the observed low conversion of consumed halogen into organic form. It is of interest to consider individually the results obtained with the three ketones studied.

(a) *Diethyl ketone.* Initial attack must occur at a CH_2 group, yielding eventually 2 : 2-di-iodopentan-3-one. On hydrolysis, this compound will give pentane-2 : 3-dione which, by analogy with 1-phenylpropane-1 : 2-dione,[4] may undergo oxidation to acetic and propionic acids. Simultaneously, in view of the presence of a $CH_3{\cdot}CO$ group in the intermediate α-diketone, some iodoform will be formed by a normal haloform reaction. The overall reactions may thus include the following :

$$Et_2CO + 3I_2 + 8NaOH = Me{\cdot}CO_2Na + Et{\cdot}CO_2Na + 6NaI + 5H_2O \quad . \quad . \quad . \quad (3)$$

$$Et_2CO + 5I_2 + 8NaOH = CHI_3 + Et{\cdot}CO{\cdot}CO_2Na + 7NaI + 6H_2O \quad . \quad . \quad . \quad . \quad (4)$$

The presence of iodo-acids in the products (including α-iodopropionic acid) suggests that, in addition to the di-iodo-ketone, some of the tri-iodo-compound $CH_3{\cdot}CI_2{\cdot}CO{\cdot}CHI{\cdot}CH_3$ is formed by further iodination of the other methylene group before hydrolysis occurs.

The observed overall iodine uptake (Fig. 1) and the low percentage conversion of consumed iodine into organic form (Table 3) suggest that oxidative fission and a haloform reaction take place concurrently, the former predominating. The widespread occurrence of oxidation with α-diketones is confirmed by analytical measurements with diacetyl (Table 3); only about 40% of the consumed iodine is converted into organic form.

(b) n-*Butyl ethyl ketone.* The two α-methylene groups will differ slightly in reactivity, but the wide variety of products (Table 2) suggests that some attack occurs in both positions. The group first halogenated in a particular molecule will preferentially suffer further attack at the same position,[5] forming an αα-di-iodo-ketone. The presence of α-iodo-acids suggests that tri-iodo-ketones are also formed as intermediates. The α-diketones formed on hydrolysis will undergo both oxidative fission, and, when a $CH_3{\cdot}CO$ group is present, a haloform reaction.

The amount of consumed halogen converted into organic form is higher than with diethyl ketone and the difference is mainly accounted for by larger quantities of iodo-acids (Table 3). This implies that with the di-iodo-intermediates from *n*-butyl ethyl ketone, further iodination occurs to a greater extent than with 2 : 2-di-iodopentan-3-one.

(c) *Diisopropyl ketone.* Initial attack must occur at a CH group with the production of a monoiodo-ketone. In order to explain the formation of α-iodo*iso*butyric acid as the

[4] Levine and Stephens, *J. Amer. Chem. Soc.*, 1950, **72**, 1642.
[5] Bell and Lidwell, *Proc. Roy. Soc.*, 1940, *A*, **176**, 88.

only acid product, this iodo-ketone must undergo fission exclusively across the $CO–CH(CH_3)_2$ bond. Since much of the consumed halogen is converted into inorganic form, an oxidative process of the following type seems to be occurring : *

$$Me_2CI{\cdot}CO{\cdot}Pr^i + I_2 + 2NaOH = Me_2CI{\cdot}CO_2H + Me_2CH{\cdot}OH + 2NaI + H_2O \quad . \; . \; (5)$$

Control experiments show that under the conditions employed, no appreciable further halogenation or oxidation of *iso*propyl alcohol takes place.

The above reaction scheme involves conversion of half the consumed iodine into organic form, and the other half into inorganic form. In practice, only about 30% of the halogen taken up is organically bound. With propiophenone,[4] 1·7 moles of hypobromite are consumed per mole of benzoic acid formed, while theoretically only 1·0 mole should be used up. By analogy, reaction (5) may also involve the consumption of more than one mole of iodine, so that more than half of the consumed halogen is used up in this way. It seems that oxidation by hypohalites is accompanied by considerable " wastage " of the active oxidising species.

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PHYSICAL CHEMISTRY DEPARTMENT, IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W.7. [*Received, July 27th*, 1956.]

* The presence of *iso*propyl alcohol among the products was tested with *p*-dimethylaminobenzaldehyde.[6] If a 1% solution of this reagent in concentrated sulphuric acid is mixed with an aqueous solution containing not less than 0·1% of *iso*propyl alcohol, a violet-red colour appears at the interface. Before the test was applied, the alkaline reaction mixture was distilled to separate neutral organic products from iodide ions, which, if present, would be oxidised to iodine, and mask the red colour.

[6] Auterhoff, *Pharm. Zentralhalle*, 1950, **89**, 293.

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298. *The Preparation of Stable Free Radicals in Solution by Means of Ionising Radiation.*

By A. J. SWALLOW.

Irradiation of a mixture of an easily reduced and an easily oxidised substance gives rise to a coupled oxidation–reduction. Methylene-blue has been irradiated in the presence of ethanol, and in strongly acid solution is reduced to the same stable semiquinone free radical as is produced by titanous chloride. Thionine also gives some free radical under these conditions, but attempts to prepare triphenylmethyl and diphenylpicrylhydrazyl by irradiation have not succeeded. Reasons are given.

A CHARACTERISTIC reaction can occur in good yield when an aqueous two-solute system is irradiated with *X*- or γ-rays, β-particles, or fast electrons : [1] one of the solutes becomes reduced while simultaneously the other becomes oxidised. Often one of the solutes is oxygen. The reaction has been most studied for aqueous solutions, but it can also occur in organic solvents,[2] the solvent itself becoming oxidised. We have used this reaction to prepare a stable free radical from methylene-blue.

The oxidisable substance used in this work was 0·5M-ethanol, the concentration of the dye being $1{\cdot}6 \times 10^{-4}$M. In order to obtain results which could be compared with those of Michaelis, Schubert, and Granick,[3] methylene-blue was dissolved in 22·9N-sulphuric acid.

To obtain a control, 4 ml. of $1{\cdot}6 \times 10^{-4}$M-methylene-blue were half-reduced under

[1] Proskurnin, Orekhov, and Barelko, *Doklady Akad. Nauk, S.S.S.R.*, 1955, **103**, 651; *Uspekhi Khim.*, 1955, **24**, 584.

[2] Piffault, Duhamel, and Longuet, *Acta Radiol.*, 1953, **39**, 64; Collinson, Dainton, and Thomson, see Collinson and Dainton, *Nature*, 1956, **177**, 1224.

[3] Michaelis, Schubert, and Granick, *J. Amer. Chem. Soc.*, 1940, **62**, 204.

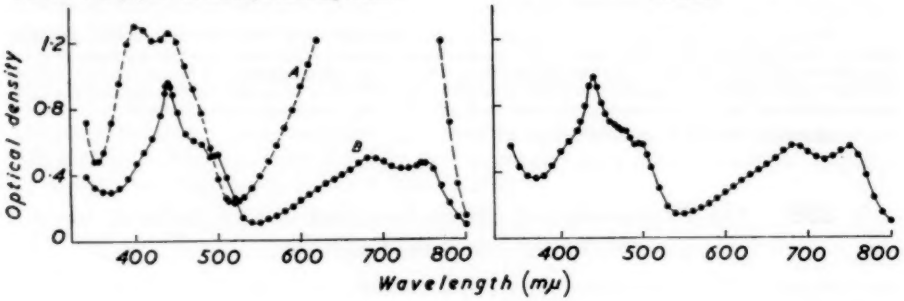
nitrogen by the addition of 0·0204 ml. of $3{\cdot}14 \times 10^{-2}$N-titanous chloride in 22·9N-sulphuric acid (standardised against a neutral methylene-blue solution). The absorption curve of the yellow solution is shown in Fig. 1 together with the curve of the original methylene-blue solution (green at this acidity). According to Michaelis *et al.*,[3] 55% of the reduction product is in the semiquinone form.

4-ml. of $1{\cdot}6 \times 10^{-4}$M-methylene-blue solution which was also 0·5M in ethanol were irradiated in the absence of air with ^{60}Co γ-rays. The change in optical density with dose was followed at 400, 440, 500, 680, and 750 mμ and, when the values approximated closely to those shown in Fig. 1*B*, the complete absorption curve was taken (Fig. 2). Air was then admitted to the solution and a few small crystals of copper sulphate added to catalyse the oxidation of the product. Within a few hours the solution had regained its original green colour, the optical densities at 400 and 440 mμ being 0·11 and 0·04 below their original values, while the optical density at 500 mμ was 0·06 above its original value.

It is clear that irradiation and titanous chloride have produced the same reduced forms of methylene-blue. The irradiation method also appears to have produced ~10% of irreversible destruction, as was noted for neutral solutions by Day and Stein.[4] From

FIG. 1. *Absorption curve of (A) methylene-blue solution and (B) the chemically reduced product.*

FIG. 2. *Absorption curve of irradiated solution.*



the dose required to produce the curve shown in Fig. 2, the overall yield of the irradiation reduction is $G = 3{\cdot}4 \pm 0{\cdot}4$ molecules of methylene-blue reduced per 100 ev absorbed. This value cannot be quoted more accurately because of difficulties in accurate titration with dilute titanous chloride.

It is suggested that oxidation or reduction induced by radiation could be applied in chemical analysis as a substitute for titration in certain cases. The general advantages of radiation as an agent are that any substance can be treated in any phase, in any solvent, at any pH, and at any temperature. Control by dose given would be exceptionally easy, and the " titration " could be carried out in a closed vessel.

Other Free Radicals.—Experiments were performed with $2{\cdot}4 \times 10^{-4}$M-thionine in 26·6N-sulphuric acid. The chemically prepared free radical showed absorption maxima at 440, 460, 480, 500, and 695 mμ but it was impossible to obtain an identical curve by irradiation in the presence of 0·5M-ethanol, a peak at 463 mμ being noted as well as peaks at 440, 500, and 695 mμ. Although some free radical is present, as was also shown by the partial restoration of colour by air, there must also be other products. The situation is further complicated by the existence of an appreciable dark reaction of ethanol with thionine.

Air-free solutions of triphenylmethyl chloride and triphenylmethane in hexane have been irradiated with *X*-rays (about 2×10^5 rad) but no colour was produced. The triphenylmethane solution was given fast-electron doses up to 3×10^6 rad, but again

[4] Day and Stein, *J. Chim. phys.*, 1955, **52**, 634.

without production of colour. Diphenylpicrylhydrazine has been *X*-irradiated in air-saturated ether, benzene, chloroform, and chloroform containing a little pyridine : although the solutions often became coloured, the colour never resembled the intense violet of diphenylpicrylhydrazyl.

To be able to make a stable free radical in the liquid phase by irradiation, it seems to be necessary that the reaction, Oxidised form + Reduced form $\rightleftharpoons$ 2 stable free radicals, takes place, the position of equilibrium being to the right. This condition is satisfied for riboflavin,[5] methylene-blue, and thionine in strongly acid solution. If this reaction does not occur, as for triphenylmethyl and diphenylpicrylhydrazyl, then any stable free radical formed would at once be irreversibly destroyed by reaction with free radicals produced from the solvent.

Experimental

Irradiation Arrangements.—*X*-Irradiations were with a Newton-Victor maximar *X*-ray therapy set operated at 190 kvp, 10 ma. The source of γ-rays was a 20-curie ^{60}Co irradiation unit. Fast-electron irradiations were with a 2 Mev Van de Graaff accelerator manufactured by the High Voltage Corporation, U.S.A.

The irradiation vessel for ^{60}Co irradiations was a modified version of the type described by Laser,[6] permitting ultraviolet absorption curves of irradiated solutions to be measured without exposure to air. The spectrophotometer cuvette was shielded during irradiation.

Dosimetry was by the ferrous sulphate method, the yield of ferrous ions oxidised being taken as 15·5 ions/100 ev absorbed.[7] To obtain the energy absorption in the strongly acid solutions used, the γ-ray dose as measured with the ferrous sulphate solution was multiplied by the density of the sulphuric acid.

Materials.—Methylene-blue and thionine were commercial samples, recrystallised from water. The moisture content was determined by drying *in vacuo* at 100° to constant weight. Other chemicals were of "AnalaR" quality.

Absorption Curves.—These were determined with 1 cm. cells in a Unicam S.P. 500 spectrophotometer, sulphuric acid being used as control. At the wavelengths used, there was no interference by titanic ions or ethanol.

The author thanks Mr. P. J. Horner for technical assistance, Mr. D. G. Lloyd for measurements of absorption curves, Professor J. S. Mitchell, F.R.S., for making irradiation facilities available, and the Chairman of Tube Investments Ltd. for permission to publish this paper.

Tube Investments Research Laboratories,
Hinxton Hall, Cambridge. [*Received, August 14th,* 1956.]

[5] Swallow, *Nature*, 1955, **176**, 793.
[6] Laser, *ibid.*, p. 361.
[7] Hochanadel, *J. Phys. Chem.*, 1952, **56**, 587; Haybittle, Saunders, and Swallow, *J. Chem. Phys.*, 1956, **25**, 1213.

299. *Cyclisation of Some Thiobenzamido-compounds.*

By Alexander Lawson and C. E. Searle.

N-Thiobenzoylsarcosine and *N*-ethyl-*N*-thiobenzoylglycine undergo ring closure in hot acid anhydrides, to give meso-ionic compounds (IV). Thiobenzamidoacetaldehyde diethyl acetal has been cyclised to the ethoxythiazoline (VI) and the thiazole (VII). Thiobenzoyl-semicarbazide and -thiosemicarbazide are cyclised to the hydroxy- (IX) or mercapto-thiadiazole (XII) or the aminothiadiazole (X), depending on the conditions.

In continuation of earlier work [1] on the preparation of α-thioacylamino-acids and their ring closure to thiazol-5-ones, preparation of some new α-thiobenzoyl-amino-acids was attempted by the Holmberg procedure.[2] Cystine reacted normally, though in poor yield, to give *NN'*-di(thiobenzoyl)cystine; the product obtained from ornithine on use of either one or two mols. of (thiobenzoylthio)acetic acid could not however be purified. Arginine gave no product, but with guanidine the reaction mixture, on treatment with bromine, gave a small yield of 3-amino-5-phenyl-1 : 2 : 4-thiadiazole, identical with the product obtained by Goerdeler and Fincke [3] using methyl thionbenzoate as acylating agent, indicating some thiobenzoylation of the guanidino-group. With sarcosine and *N*-ethylglycine, thiobenzoylation proceeded normally, though somewhat slowly in the latter case, but no thiobenzoyl derivative of *N*-phenyl-, *N*-*p*-hydroxyphenyl- or *N*-*o*-carboxyphenylglycine could be isolated.

When thiobenzoylsarcosine (I; R = Me) was heated with acetic anhydride a neutral substance $C_{12}H_{11}O_2NS$ was isolated in 70% yield. Homologous substances were formed from thiobenzoylsarcosine with propionic anhydride, and from *N*-ethyl-*N*-thiobenzoylglycine with acetic anhydride. The compound $C_{12}H_{11}O_2NS$, on hydrolysis with hydrochloric acid, gave sarcosine hydrochloride, hydrogen sulphide, and acetic and benzoic acids, indicating that no group migration had occurred in its formation. The analytical results, and the ready solubility in organic solvents, showed that the compound was not a thiazolium acetate analogous to the type suggested by O'Brien and Niemann [4] to account for the high van't Hoff *i* factor given by benzoylsarcosine in concentrated sulphuric acid. The substance, which is under further investigation, gave a phenylhydrazone and an unstable dinitrophenylhydrazone. It has therefore been designated as ψ-4-acetyl-3-methyl-2-phenylthiazol-5-one (IV; R = R' = Me) and doubtless belongs to the mesoionic class of compounds of which the sydnones [5,6] and anhydro-pyridine- and -quinoline-2-thiolacetic acids [7] are examples. The compound probably arises as a result of the reaction sequence (I)—(IV) in which ring closure of the mixed anhydride (II) is followed by *C*-acylation as in the Dakin and West reaction,[8] but in this case without the decarboxylation that normally takes place with an oxazolone. Such acylation is comparable to the *C*-halogenation of sydnones.[6] It is possible that in the decarboxylative acylation of *N*-alkylated amino-acids such as sarcosine an unstable mesoionic ψ-oxazolone intermediate is involved rather than the oxazolonium cation suggested by Cornforth and Elliot.[9]

Through the kindness of Dr. S. A. Barker and Dr. D. H. Whiffen of the Chemistry

[1] Jepson, Lawson, and Lawton, *J.*, 1955, 1791.
[2] Holmberg, Svedberg Anniversary Vol., Uppsala, 1944, p. 299.
[3] Goerdeler and Fincke, *Chem. Ber.*, 1956, **89**, 1033.
[4] O'Brien and Niemann, *J. Amer. Chem. Soc.*, 1950, **72**, 5348.
[5] Earl and Mackney, *J.*, 1935, 899.
[6] Baker, Ollis, and Poole, *J.*, 1950, 1542.
[7] Duffin and Kendall, *J.*, 1951, 734.
[8] Dakin and West, *J. Biol. Chem.*, 1928, **78**, 91.
[9] Cornforth and Elliot, *Science*, 1950, **112**, 534.

XUM

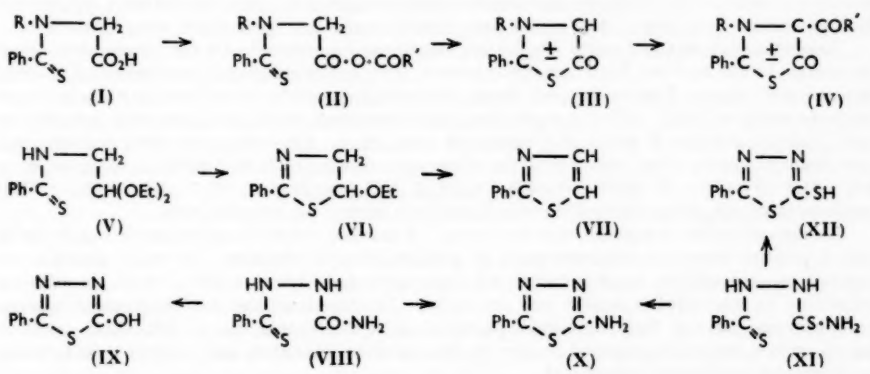
Department, University of Birmingham, the infrared spectrum of ψ-4-acetyl-3-methyl-2-phenylthiazole-5-one (IV; R = R′ = Me) has been examined. The highly conjugated nature of the carbonyl group in position 4, suspected because of the difficulty of preparing the usual ketonic derivatives, is confirmed by the large displacement of the carbonyl absorption from 1725—1705 cm.$^{-1}$ in saturated aliphatic ketones to 1644 cm.$^{-1}$ in this substance.

Attempts to open the ring in the compound (IV; R = R′ = Me) resulted in gross decomposition. Though resistant to catalytic hydrogenation at atmospheric pressure and unaffected by ammonia in dioxan at 100° (in contrast to thiazolones), the substance reacted with benzylamine and aniline with loss of the sulphur to give unidentified crystalline products.

2-Thiobenzamidoethanol and 3-thiobenzamidopropanol, prepared from the amino-alcohols, were readily dehydrated to 2-phenylthiazoline and 5 : 6-dihydro-2-phenyl-1 : 3-thiazine.

Thiobenzamidoacetaldehyde diethyl acetal (V), prepared readily from aminoacetal, lost one mol. of ethanol under mild dehydrative conditions, giving 5-ethoxy-2-phenylthiazoline (VI), and a second mol. under more vigorous conditions, giving 2-phenylthiazole (VII).

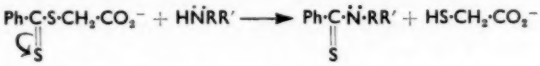
1-Thiobenzoylsemicarbazide (VIII), when heated alone or with hot concentrated hydrochloric or polyphosphoric acid, gave 2-hydroxy-5-phenyl-1 : 3 : 4-thiadiazole (IX) by elimination of ammonia; with acetic anhydride the corresponding acetyl derivative was obtained; with acetyl chloride, on the other hand, cyclisation took place with loss of water to give 2-amino-5-phenyl-1 : 3 : 4-thiadiazole (X), prepared by Young and Eyre [10] by oxidation of benzylidenethiosemicarbazone with ferric chloride. Cyclisation of 1-thiobenzoylthiosemicarbazide (XI) likewise could proceed by alternative routes: loss of hydrogen sulphide to give (X) or loss of ammonia to give 2-mercapto-5-phenyl-1 : 3 : 4-thiadiazole (XII).



Rates of reaction of (thiobenzoylthio)acetic acid with different amino-compounds vary greatly. In the absence of steric hindrance of the approach of the amino-nitrogen atom to the thion-carbon atom of the (thiobenzoylthio)acetic acid, the ease of reaction depends largely on the electronegativity of the amino-nitrogen atom. However, reaction occurred very slowly or not at all with 2-amino-2-methylpropanol and 2-amino-2-methylpropane-1 : 3-diol in which the amino-group is attached to a quaternary carbon atom, and this is attributed to steric factors, which prevent close approach of the reacting groups. Similar considerations presumably apply in the case of α-amino*iso*butyric acid, which was found by Jepson *et al.*[1] to be very resistant to thiobenzoylation. Thiobenzoylation occurred

[10] Young and Eyre, *J.*, 1901, 54.

rapidly with two amino-alcohols (2-aminoethanol and 3-aminopropanol) in which those steric relations do not occur.



Owing to the exceptional rapidity with which it is thiobenzoylated morpholine may be used to test for the presence of unchanged (thiobenzoylthio)acetic acid in a reaction mixture, or to remove it before liberation of a thiobenzamido-acid by acidification.

When thiobenzoylation is slow it is accompanied by side reactions which result in small yields. In such cases some benzaldehyde was usually observed as a by-product, and the mixture remained dark. Hydrogen sulphide was sometimes evolved. It is possible that thiobenzoylation with methyl thionbenzoate,[1] although slower and less convenient, would be more satisfactory with the less reactive amino-compounds.

The action of silver nitrate on new thiobenzoyl derivatives in aqueous alcohol was examined. Silver sulphide was usually formed rapidly in the cold when the group ·CS·NH· was present, although thiobenzoyl-cystine, -semicarbazide, and -thiosemicarbazide did not react appreciably until the mixture was heated. The presence of hydrogen on the nitrogen atom adjacent to the thion group is not essential, however, since thiobenzoyl-sarcosine reacted readily in the cold. Thiobenzoyl-piperidine and -morpholine reacted only slowly at 100°, which may indicate initial hydrolysis.

Experimental

Thiobenzoylation of Amino-acids.—(Thiobenzoylthio)acetic acid, m. p. 125—126°, was prepared by Crawhall and Elliot's method [11] in yields up to 53%. The alkaline solution obtained after addition of sodium chloroacetate and refluxing usually gave a crystalline product when acidified at 0° with hydrochloric acid, and extraction from a benzene solution into alkali was thus avoided. On the larger scale used in the present work crystallisation from chloroform–light petroleum (b. p. 100—120°) rather than from benzene–light petroleum was preferred.

Thiobenzoylation was carried out by the Holmberg procedure.[2] Of the amino-acids whose thiobenzoylation had not been already reported, only sarcosine gave a good yield of its thiobenzoyl derivative. Cystine reacted slowly with (thiobenzoylthio)acetic acid, a little hydrogen sulphide being evolved. After 3 weeks the pale red solution was neutralised with hydrochloric acid, yielding a dark oil which was extracted with ether. Crystallisation from benzene–light petroleum of the oil after removal of the ether gave needles of NN'-*dithiobenzoylcystine*, m. p. 117—118° (Found : C, 58·0; H, 4·5. $C_{20}H_{20}O_4N_2S_2$ requires C, 57·7; H, 4·8%). With aqueous-ethanolic silver nitrate, silver sulphide was formed on warming only.

Thiobenzoylation of arginine was very slow. A marked smell of benzaldehyde was observed and a positive test was obtained with 2 : 4-dinitrophenylhydrazine. No solid product was isolated on acidification or after treatment with acetic anhydride at 100°. With an excess of guanidine hydrochloride reaction was also slow. Treatment of the red supernatant solution with bromine gave a little 3-amino-5-phenyl-1 : 2 : 4-thiadiazole, m. p. 132—134°, alone or mixed with a specimen prepared by Dr. F. Kurzer from guanidine and methyl thionbenzoate by Goerdeler and Fincke's method.[3]

Thiobenzoylsarcosine.—A solution containing (thiobenzoylthio)acetic acid (2·1 g., 1 mol.), sarcosine (1·0 g., 1·1 mol.), and sodium hydroxide (0·8 g., 2 mol.) in 25 ml. of water was set aside at room temperature for 4 days. The light red cloudy solution, smelling of benzaldehyde, was filtered, chilled, and acidified with hydrochloric acid. The crude oil soon solidified. Its solution in chloroform was washed with water and evaporated to small bulk. Addition of light petroleum gave *thiobenzoylsarcosine* (1·46 g., 70%), pale yellow tablets (from ethyl acetate–light petroleum), m. p. 152—153° (decomp.) when inserted at 130° (Found : C, 57·8; H, 5·2; N, 6·7. $C_{10}H_{11}O_2NS$ requires C, 57·4; H, 5·3; N, 6·7%).

N-*Ethyl*-N-*thiobenzoylglycine.*—Thiobenzoylation of *N*-ethylglycine occurred much less readily than with sarcosine. After 5 days, the solution, which was still dark red but gave no

[11] Crawhall and Elliot, *J.*, 1951, 2071.

product with morpholine, was filtered, chilled, and acidified. The resultant oil was extracted with chloroform, washed with water, dried, and evaporated. The residue gave *N-ethyl-N-thiobenzoylglycine*, thick blades (26%), m. p. 136—137°, from ethyl acetate–light petroleum (Found: C, 59·5; H, 5·9. $C_{11}H_{13}O_2NS$ requires C, 59·2; H, 5·8%). With *N-p*-hydroxyphenylglycine only a gum was obtained.

Reaction of Thiobenzoylsarcosine and N-Ethyl-N-thiobenzoylglycine with Acid Anhydrides.—Thiobenzoylsarcosine (1·0 g.) was warmed on the steam-bath with acetic anhydride (15 c.c.), rapidly darkening. After 1 hr. the excess of anhydride was removed under reduced pressure, then xylene was twice added and removed similarly. The dark residue of *ψ-4-acetyl-3-methyl-2-phenylthiazol-5-one* (77%) crystallised from aqueous ethanol (charcoal), then from chloroform or ethyl acetate–light petroleum as a light yellow solid, m. p. 134—135° [Found: C, 61·6; H, 4·8; N, 5·9; S, 14·1%; *M* (Rast), 232. $C_{12}H_{11}O_2NS$ requires C, 61·7; H, 4·7; N, 6·0; S, 13·7%; *M*, 233] $\lambda_{max.}$ 2440, 2800, 3570 Å (ε 10,240, 9900, 11,020) in EtOH.

If the temperature was raised to 140° and air replaced by nitrogen, the same product was obtained in 69% yield. In the presence of 3-methylpyridine (10 ml.) some carbon dioxide was evolved but only the above compound (22%) was isolated.

A homologous substance was obtained by treating thiobenzoylsarcosine similarly with propionic anhydride. The mass remaining after removal of the anhydride was extracted several times with light petroleum (b. p. 80—100°). *ψ-4-Propionyl-3-methyl-2-phenylthiazol-5-one*, yellow needles, had m. p. 109—110° (61%) (Found: C, 63·0; H, 5·05. $C_{13}H_{13}O_2NS$ requires C, 63·2; H, 5·25%).

When *N*-ethyl-*N*-thiobenzoylglycine in acetic anhydride was heated at 100° the mixture darkened slowly. The *ψ-4-acetyl-3-ethyl-2-phenylthiazol-5-one*, isolated as above, crystallised from aqueous ethanol as pale yellow prismatic needles, m. p. 104—105° (Found: C, 63·0; H, 5·2. $C_{13}H_{13}O_2NS$ requires C, 63·2; H, 5·25%).

Reactions of ψ-4-Acetyl-3-methyl-2-phenylthiazolone.—The compound dissolved readily in ethyl acetate and chloroform, and sparingly in ether and light petroleum. It was insoluble in cold dilute acids and bases. The *phenylhydrazone*, prepared in aqueous acetic acid, had m. p. 218° (prismatic needles from ethanol) (Found: C, 66·5; H, 5·2. $C_{18}H_{17}ON_3S$ requires C, 66·8; H, 5·3%). A sparingly soluble 2:4-dinitrophenylhydrazone, prepared in ethanol containing a drop of sulphuric acid, decomposed on recrystallisation.

(a) *With bases.* Attempts to remove the acetyl group by alkaline hydrolysis gave no isolable product. The compound was recovered unchanged after being heated with ammonia in dioxan at 100° (cf. thiazolones [1]).

When the substance (0·5 g.) was heated with benzylamine (2 ml.) the mixture became dark green at about 90° and evolved hydrogen sulphide and a garlic-like odour. After 0·5 hr. at 130° the whole was poured into iced water. The sticky solid gave, from ethyl acetate–light petroleum, an unidentified sulphur-free *substance* (0·23 g.) as colourless needles, m. p. 168—169° (Found: C, 74·9; H, 6·5; N, 11·4. $C_{15}H_{16}ON_2$ requires C, 75·0; H, 6·7; N, 11·7%). The acetyl group was removed during the reaction, since the 4-propionyl analogue gave the same substance.

A similar yield was obtained by refluxing the reactants in water until no more hydrogen sulphide was evolved (6 hr.); but carrying out the reaction in boiling xylene under nitrogen gave a less easily purified product.

With aniline, hydrogen sulphide was not evolved until 130—140°, the solution becoming green at 150—160°. After 1 hr. at 160—170° the mixture was poured into dilute hydrochloric acid, the resulting sticky solid being washed and dried in chloroform. The *product* crystallised as stout needles, m. p. 250—252° (decomp.), from ethyl acetate–light petroleum. Analysis agreed with the simple replacement of S by $N{\cdot}C_6H_5$ (38%) (Found: C, 74·1; H, 5·4. $C_{18}H_{16}O_2N_2$ requires C, 74·0; H, 5·5%). Refluxing in xylene for 2·5 hr. under nitrogen gave the same compound (59%). This substance was more basic than that obtained from benzylamine. Treatment of a chilled solution in dilute hydrochloric acid with sodium nitrite caused separation of another substance as needles, m. p. 194—195°, from aqueous methanol or ethyl acetate–light petroleum (Found: C, 68·6; H, 4·6%).

(b) *With acid.* Warming the thiazolone gently in concentrated hydrochloric acid gave a pale yellow solution, which after 3 hr. at 100° yielded benzoic acid. Evaporation of the filtrate under reduced pressure gave sarcosine hydrochloride, m. p. (after precipitation with dry ether from absolute ethanol) 166—169°, mixed m. p. 166—170°.

XUM

Thiobenzamido-alcohols and -acetals and Their Cyclisation.—2-Thiobenzamidoethanol, formed rapidly in 81% yield on addition of a slight excess of 2-aminoethanol to aqueous sodium (thiobenzoylthio)acetate at room temperature, had m. p. 93—94° (from chloroform–light petroleum) (Goldberg and Kelly [12] give m. p. 96°) (Found: C, 59·7; H, 6·1. Calc. for $C_9H_{11}ONS$: C, 59·8; H, 6·1%).

Ring-closure to 2-phenylthiazoline occurred readily. The picrate, tablets from ethyl acetate, had m. p. 172—173·5° (Gabriel and Leupold [13] gave m. p. 173—174°) (Found: C, 45·7; H, 3·2. Calc. for $C_{15}H_{12}O_7N_4S$: C, 45·9; H, 3·1%). Cyclisation was carried out by gently warming the compound with phosphoric oxide (yield 75%), heating it with polyphosphoric acid on the steam-bath for 1 hr. (67%), or storage overnight in cold concentrated hydrochloric acid (77%), the mixture in each case being added to excess of water and extracted with ether after basification.

Attempted dehydration of 2-thiobenzamidoethanol by acetic anhydride at 100° gave *2-thiobenzamidoethyl acetate* as a red oil which from ether–light petroleum gave light yellow prismatic rods, m. p. 67—68° (65%) (Found: C, 59·2; H, 5·8. $C_{11}H_{13}O_2NS$ requires C, 59·3; H, 6·0%). The *benzoate* (53%) was obtained by using benzoyl chloride in 3-methylpyridine at 0° and had m. p. 125—126° (from chloroform–light petroleum) (Found: C, 67·4; H, 5·3. $C_{16}H_{15}O_2NS$ requires C, 66·9; H, 5·3%).

3-Aminopropanol was thiobenzoylated less readily than 2-aminoethanol. The red oil which separated was, after 18 hr., dissolved in ether, washed, and dried. Evaporation to small bulk and addition of light petroleum gave *3-thiobenzamidopropanol*, pale yellow leaflets, m. p. 69—70·5° (79%) (Found: C, 61·7; H, 6·7. $C_{10}H_{13}ONS$ requires C, 61·5; H, 6·7%). Its solution in cold concentrated hydrochloric acid, on being kept overnight, diluted, and treated with excess of sodium carbonate, gave 5 : 6-dihydro-2-phenyl-1 : 3-thiazine as an oil. This gave a *picrate*, m. p. 183—185°, from ethanol (Found: C, 47·4; H, 3·4. $C_{16}H_{14}O_7N_4S$ requires C, 47·3; H, 3·45%). The mercuric chloride complex had m. p. 141—143° (Pinkus [14] gave m. p. 140—142°).

Thiobenzoyl derivatives of 2-amino-2-methylpropanol and 2-amino-2-methylpropane-1 : 3-diol could not be prepared by the Holmberg procedure, even by using a considerable excess of the amino-alcohols. The benzaldehyde-like odour always observed in such experiments was in the former case shown to be due to benzaldehyde, identified as the semicarbazone.

On addition of a slight excess of aminoacetaldehyde diethyl acetal to aqueous sodium (thiobenzoylthio)acetate with stirring, *thiobenzamidoacetaldehyde diethyl acetal* (89%) rapidly separated; it had m. p. 69—70° (from ethyl acetate–light petroleum) (Found: C, 61·4; H, 7·65. $C_{13}H_{19}O_2NS$ requires C, 61·7; H, 7·5%). Warming with concentrated hydrochloric acid yielded 5-ethoxy-2-phenylthiazoline as an oil, giving the *picrate*, m. p. 163—164°, from ethanol (95%) (Found: C, 46·5; H, 3·6. $C_{17}H_{16}O_8N_4S$ requires C, 46·8; H, 3·6%). The same base was obtained by ring-closure with polyphosphoric acid at 100° (54%). Ring-closure with polyphosphoric acid at 180° or with hot phosphoric oxide however gave 2-phenylthiazole, also isolated as the picrate, m. p. 123—124° from aqueous ethanol (Hubacher [15] gave m. p. 124—125°). The lower yields (50% and 27% respectively) were probably caused by the high solubility of the picrate in ethanol.

No thiobenzoyl derivative of methylaminoacetaldehyde diethyl acetal could be isolated.

Thiobenzoylsemicarbazides and Their Cyclisation.—Semicarbazide was thiobenzoylated in the usual way, a slight excess of semicarbazide hydrochloride being used. In the presence of only 2 mols. of sodium hydroxide, the product, which was soluble in excess of alkali, separated from the reaction mixture. After 6 hr. at room temperature *1-thiobenzoylsemicarbazide* (68%) was crystallised from ethyl acetate–light petroleum as light yellow leaflets, m. p. 158—159° (Found: C, 49·0; H, 4·6. $C_8H_9ON_3S$ requires C, 49·2; H, 4·6%).

In refluxing concentrated hydrochloric acid 1-thiobenzoylsemicarbazide was quickly converted into *2-hydroxy-5-phenyl-1 : 3 : 4-thiadiazole*, m. p. 146—148° (from ethanol) (64%) (Found: C, 53·9; H, 3·4; N, 15·6. $C_8H_6ON_2S$ requires C, 53·9; H, 3·4; N, 15·7%). The thiadiazole, which was soluble in sodium carbonate, was also obtained by using polyphosphoric acid at 140° (88%) or heating thiobenzoylsemicarbazide alone at 190° (83%).

[12] Goldberg and Kelly, *J.*, 1948, 1919.
[13] Gabriel and Leupold, *Ber.*, 1898, **31**, 2833.
[14] Pinkus, *Ber.*, 1893, **26**, 1077.
[15] Hubacher, *Annalen*, 1890, **259**, 228.

Treatment of thiobenzoylsemicarbazide with acetic anhydride at 100° for 2 hr., followed by dilution with acetone and pouring on ice, gave *2-acetoxy-5-phenyl-1 : 3 : 4-thiadiazole* (75%), m. p. 117—119° (from aqueous ethanol) (Found : C, 54·2; H, 3·5; N, 12·6. $C_{10}H_8O_2N_2S$ requires C, 54·5; H, 3·6; N, 12·7%). The same compound was produced by the action of acetyl chloride on the semicarbazide in 3-methylpyridine, but in the absence of a base acetyl chloride at room temperature gave 2-amino-5-phenyl-1 : 3 : 4-thiadiazole, m. p. 224—225° (oil-bath), 240—241° (block) (from chloroform–light petroleum) (Young and Eyre [10] gave m. p. 222—223°). Mixed with a specimen prepared by their procedure it had m. p. 224—226° (Found : C, 54·0; H, 4·1. Calc. for $C_8H_7N_3S$: C, 54·2; H, 3·95%). When the acetyl chloride mixture was poured on ice a strong smell of benzoyl chloride was observed.

1-Thiobenzoylthiosemicarbazide was prepared in the usual way. The bright yellow solid (69%), which was too unstable to be purified by crystallisation or by dissolution in sodium hydrogen carbonate solution, was freed from traces of unchanged (thiobenzoylthio)acetic acid by washing with cold ether (Found : C, 45·8; H, 4·75; N, 20·3. $C_8H_9N_3S_2$ requires C, 45·7; H, 4·3; N, 19·9%). At 125—128° it became colourless with the elimination of hydrogen sulphide, the m. p. recorded being that of the resulting 2-amino-5-phenyl-1 : 3 : 4-thiadiazole (above), which was most conveniently formed by boiling thiobenzoylthiosemicarbazide with water until no more hydrogen sulphide was evolved (63%). It formed a very sparingly soluble *picrate*, felted needles (from aqueous acetone), m. p. 268—271° (decomp.) (block) (Found : C, 41·0; H, 2·5. $C_{14}H_{10}O_7N_6S$ requires C, 41·4; H, 2·5%).

Treating 1-thiobenzoylthiosemicarbazide with cold concentrated hydrochloric acid gave at once a quantitative yield of *2-mercapto-5-phenyl-1 : 3 : 4-thiadiazole*, pale yellow crystals (from aqueous ethanol), m. p. 224—225·5° (block) (Found : C, 49·7; H, 3·3; N, 14·6. $C_8H_6N_2S_2$ requires C, 49·5; H, 3·1; N, 14·4%). This was soluble in aqueous sodium hydroxide and gave a yellow colour with sodium nitroprusside, gave no precipitate with mercuric chloride, and with silver nitrate gave a slight precipitate of a silver salt but no silver sulphide on warming.

Refluxing the thiol with benzyl chloride and sodium hydrogen carbonate in 70% aqueous ethanol for 4 hr. afforded *2-benzylthio-5-phenyl-1 : 3 : 4-thiadiazole*, needles (from aqueous ethanol), m. p. 108—109° (91%) (Found : C, 63·4; H, 4·2. $C_{15}H_{12}N_2S_2$ requires C, 63·4; H, 4·2%).

Thiobenzoylation of Secondary Amines.—Addition of morpholine in slight excess to aqueous sodium (thiobenzoylthio)acetate caused almost instantaneous decolorisation of the solution and precipitation of solid thiobenzoylmorpholine (91%), needles (from aqueous ethanol), m. p. 137—138° (McMillan and King [16] gave m. p. 137—138·5°) (Found : C, 64·1; H, 6·4. Calc. for $C_{11}H_{13}ONS$: C, 63·8; H, 6·3%). The compound was also formed rapidly on addition of morpholine to (thiobenzoylthio)acetic acid in hot water or dissolution of (thiobenzoylthio)-acetic acid in morpholine.

When twice the theoretical amount of piperidine was added to aqueous sodium (thiobenzoylthio)acetate decolorisation soon occurred with the separation of thiobenzoylpiperidine as an oil which later crystallised. The product had m. p. 61—62° after crystallisation from warm ethanol, then ether–light petroleum (Bergmann [17] gave m. p. 63—64°) (Found : C, 70·2; H, 7·2. Calc. for $C_{12}H_{15}NS$: C, 70·25; H, 7·3%).

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ROYAL FREE HOSPITAL SCHOOL OF MEDICINE,
8, HUNTER STREET, LONDON, W.C.1.

[*Received, September 28th,* 1956.]

[16] McMillan and King, *J. Amer. Chem. Soc.*, 1948, **70**, 4143.
[17] Bergmann, *Ber.*, 1920, **53**, 979.

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300. *Autoxidation of Polyphenols. Part III.* Autoxidation in Neutral Aqueous Solution of Flavans related to Catechin.*

By D. E. Hathway and J. W. T. Seakins.

The formation of polymers and hydrogen peroxide during the autoxidation of catechin and of related 3′ : 4′-dihydroxyflavans has been studied by measurement of oxygen adsorption, and by elementary analyses, absorption spectra, and colour reactions of the dialysed polymers. The evidence obtained, together with that provided by spectroscopic study of intermediates produced by silver oxide oxidation, supports the theory that tannin formation from catechin occurs by polymerisation through quinones (Part II). Whereas polymerisation through quinones of catechin and 5 : 7 : 3′ : 4′-tetrahydroxyflavan involves the phloroglucinol residue, oxidative coupling of 5 : 7-di-*O*-methylcatechin and 3′ : 4′-dihydroxyflavan resembles that of catechol. The relevance of catechin autoxidation to the biogenesis of phlobatannins is considered.

In Part II, a manometric study of catechin autoxidation, and the spectroscopic study of an intermediate obtained by silver oxide oxidation, supported the theory that tannin formation from catechin occurs by polymerisation through quinones.

Consideration of the data accumulated from autoxidation studies on simpler substances (Tables 1 and 2 and Figures 1 and 2) confirms that catechin autoxidation involves polymerisation of quinones, but that constitutional differences modify this process in the case of the flavans.

Manometry of the Polyhydroxyflavans.—Free hydroxyl groups in the 3′- and the 4′-positions (Table 1) cause an accumulation of hydrogen peroxide which is associated with quinone formation (cf. Part II). 5 : 7-Dihydroxy- and 5 : 7-dihydroxy-3′ : 4′-dimethoxy-flavans lack vicinal hydroxyl groups and can be recovered almost quantitatively after several days' autoxidation. Adsorption of oxygen in excess of the theoretical 1 mol. may be attributed to (1) manometric difficulties associated with protracted experiments (cf. the rapid oxidation of 5 : 6-dihydroxyindoles to melanins [1]), (2) two oxidative couplings per mole of *o*-quinone, or (3) oxidative degradation of some of the *o*-quinonoid residues with incorporation of more oxygen in the polymer. The possibility of experimental error in the total adsorption readings is the most likely, for multiple coupling (2) would lead to polymers exhibiting general light absorption like melanin, but some oxidative degradation of *o*-quinones by peroxide may take place even under the mild conditions of autoxidation.[1] Since the maximum rates of oxygen adsorption were determined at an early stage in these experiments, their accuracy is not subject to the same limitations. The similar manometric results for catechin and 5 : 7 : 3′ : 4′-tetrahydroxyflavan autoxidation are consistent with a common mechanism. In the present study the suggestion [2] that in acid solution catechin may polymerise as a reactive flaven has been tested by comparison of the behaviour of catechin and 5 : 7 : 3′ : 4′-tetrahydroxyflavan. Autoxidation of the bifunctional catechin molecule is slow, since oxidation to quinone is inhibited by phenols,[3] and the faster rate of autoxidation of the 5 : 7-di-*O*-methyl derivative agrees with this principle. Since the rate of autoxidation of 5 : 7 : 3′ : 4′-tetrahydroxyflavan is faster than that of catechin, the secondary alcoholic group in catechin exerts a steric factor [4] which lowers the rate of autoxidation, and the relative rates of autoxidation of 5 : 7-di-*O*-methylcatechin and 3′ : 4′-dihydroxyflavan are consistent with this view.

* Part I, *J.*, 1957, 519. The paper by Hathway and Seakins (*Nature*, 1955, **176**, 218) is considered to be Part II.

[1] Beer, Broadhurst, and Robertson, *J.*, 1954, 1947.
[2] Freudenberg and Weinges, *Annalen*, 1955, **590**, 140.
[3] James, Snell, and Weissberger, *J. Amer. Chem. Soc.*, 1938, **60**, 2084.
[4] Bu'Lock and Harley-Mason, *J.*, 1951, 709.

Polymer Analysis.—To obtain correspondence between the analyses of the dialysed oxidation products (Table 2) and those of true polymers, a calculated addition of 1·7—3·3 moles of water per mole of starting materials must be made, but a similar assumption was made for the melanins.[1] Evidence for hydration is found in the persistence of a strong spectral band at 1627—1635 cm.$^{-1}$ after protracted drying of the polymer at 70° *in vacuo*. Hergert and Kurth [5] using similar evidence found that (+)-catechin retained water after being dried at 115° *in vacuo* for several weeks. Unfortunately retention of water by the polymers prevents an examination of the fundamental carbon–oxygen stretching vibration

FIG. 1. *Absorption spectra of polymers from (A) catechol, (B) 5 : 7-di-O-methylcatechin, and (C) 3′ : 4′-dihydroxyflavan.*

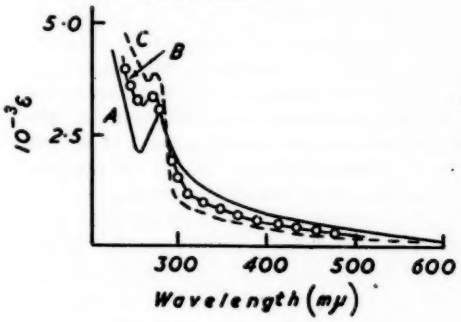

FIG. 2. *Absorption spectra of polymers from (I) catechin and (II) 5 : 7 : 3′ : 4′-tetrahydroxyflavan.*

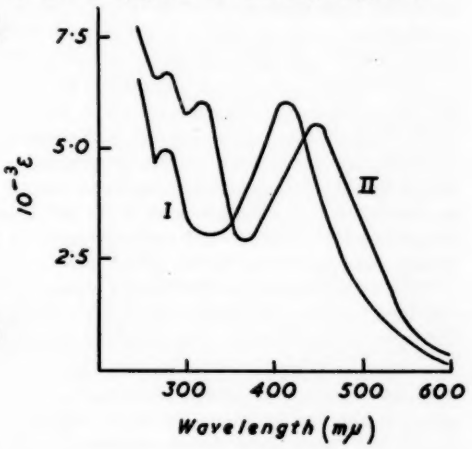

TABLE 1. *Oxygen adsorption by polyhydroxyflavans at 35°.*

	Oxygen uptake [a]	Residual peroxide [a]	Oxygen balance [a]	Maximum rate [b]	Reaction period [c]
Catechin	1·59	0·38	1·40	$5·6 \times 10^{-4}$	2
5 : 7-Di-*O*-methylcatechin	2·00	0·39	1·80	$8·4 \times 10^{-3}$	1·25
5 : 7-Dihydroxyflavan	—	0	—	$1·9 \times 10^{-4}$	>7
5 : 7-Dihydroxy-3′ : 4′-dimethoxyflavan	—	0	—	$5·3 \times 10^{-4}$	>7
3′ : 4′-Dihydroxyflavan	1·90	0·37	1·70	$1·2 \times 10^{-2}$	1·25
5 : 7 : 3′ : 4′-Tetrahydroxyflavan	2·00	0·80	1·60	$3·0 \times 10^{-3}$	1·25

The corresponding autoxidation of catechol, maximum rate $5·6 \times 10^{-3}$ mole/min., was complete in 1 day.

[a] moles. [b] mole/min. [c] days.

TABLE 2. *Polymer analyses.*

	Found, %		Calc., %		
Polymers from :	C	H	C	H	Empirical formula
Catechin	52·6	4·6	53·0	4·7	$C_{15}H_{10}O_6,3H_2O$
5 : 7-Di-*O*-methylcatechin	57·7	5·5	57·7	5·5	$C_{17}H_{18}O_6,2·2H_2O$
3′ : 4′-Dihydroxyflavan	67·1	5·4	67·1	5·4	$C_{15}H_{14}O_3,1·7H_2O$
5 : 7 : 3′ : 4′-Tetrahydroxyflavan	54·5	5·1	54·6	5·1	$C_{15}H_{10}O_5,3·3H_2O$

in the 1650—1720 cm.$^{-1}$ region. Since these oxidation polymers are hydrated and difficult to analyse, no acceptable conclusion may be drawn from the analyses regarding the secondary oxidation of some of the *o*-quinone units, or the extent of multiple coupling of *o*-quinone.

Polymer Properties.—Since the acid-catalysed polymer from catechin gives a vanillin reaction (Part II), the application of this reaction to the present polymers is justified.

[5] Hergert and Kurth, *J. Org. Chem.*, 1953, **18**, 521.

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Unlike the corresponding monomers, the polymers from catechin and from 5 : 7 : 3′ : 4′-tetrahydroxyflavan do not react with vanillin reagent, whereas that from 5 : 7-di-*O*-methylcatechin gives a strongly positive reaction.

Absorption Spectra.—The absorption spectra of the polymers are of two classes. The polymers from 3′ : 4′-dihydroxyflavan and 5 : 7-di-*O*-methylcatechin have spectra almost identical with that of the polymer from catechol (Fig. 1), whereas the polymers from catechin and 5 : 7 : 3′ : 4′-tetrahydroxyflavan have spectra compatible with that expected for a polymer with a repeated quinone unit (Fig. 2). Compounds of the first class exhibit phenolic absorption at 280 mμ, and general absorption at 300—600 mμ. The similarity of the spectra of the polymers from 5 : 7-di-*O*-methylcatechin and catechol is consistent with a common mechanism of autoxidation. Methoxyl groups in the 5- and the 7-position of 5 : 7-di-*O*-methylcatechin therefore inhibit the head-to-tail polymerisation of the quinones. Substances of the second class exhibit a well-defined maximum at 410—430 mμ, and two maxima at shorter wavelengths.

Discussion.—Since polymerisation through quinones of catechol and 3′ : 4′-dihydroxyflavan involves catechol residues, the similarity of the spectra of the polymers obtained with that of the polymer from 5 : 7-di-*O*-methylcatechin is consistent with a common autoxidation mechanism. The possibility of some degree of head-to-tail polymerisation involving the phloroglucinol residues cannot be precluded from a consideration of the autoxidations of catechin and 5 : 7 : 3′ : 4′-tetrahydroxyflavan, however, and it is now suggested that head-to-tail polymer units of these substances may account for the profound difference in spectrum of the polymers from those of the catechol polymers.

For two decades the Heidelberg school has maintained [6,7] that the phlobatannins from the barks of *Acacia mollissima*, birch, chestnut (*Castanea sativa*), Eucalypts, mangrove, oak, spruce, and willow, and from the heartwood of *Acacia catechu* and *quebracho* trees are catechins, polymerised *post-mortem* under the influence of the plant acids. Two mechanisms have been considered. According to the first,[6] ring fission gives a secondary benzyl alcohol, and carbon atom 2 then condenses with carbon atom 6 or 8 of another molecule to afford a bifunctional dimer, capable of further polymerisation. More recently, Freudenberg [8] has suggested that catechin may react as a pair of tautomeric diphenylpropenes which are involved in the first stage of a styrene polymerisation.[9] On the assumption that phlobatannins are indeed formed by polymerisation of catechin, then the enzymic autoxidation of catechin by polymerisation through quinones is a more attractive hypothesis, especially since the acid-catalysed reaction suggested by Freudenberg requires low pH (<2) and high temperature (>50°).

Polyhydroxyflavans.—The Simonis synthesis of flavanones from phloroglucinol and cinnamoyl chloride derivatives has been extensively studied,[10] and despite the customary low yields this reaction has been used for the preparation of eriodictyol and 5 : 7-dihydroxy-3′ : 4′-dimethoxyflavanone. Improved yields were obtained, however, by the use of ether instead of nitrobenzene as reaction medium. Clemmensen reduction at room temperature [11] of the flavanones gave the 5 : 7 : 3′ : 4′-tetrahydroxy- and 5 : 7-dihydroxy-3′ : 4′-dimethoxy-flavans. Partial methylation of (+)-catechin by means of methyl sulphate and aqueous alkali in the presence of excess of sodium metaborate [12] gave 5 : 7-di-*O*-methyl-(+)-catechin. 3′ : 4′-Dihydroxyflavan was prepared from 3 : 4 : 2′-trihydroxychalcone by catalytic hydrogenation, followed by benzoylation, and lithium aluminium

[6] Freudenberg and Maitland, *Annalen*, 1934, **510**, 193; *Collegium*, 1934, **776**, 656.
[7] Mayer and Bauni, *Das Leder*, 1956, **7**, 35; Schmidt and Mayer, *Angew. Chem.*, 1956, **68**, 103.
[8] Freudenberg, *Sci. Proc. Roy. Dublin Soc.*, 1956, **27**, 153.
[9] Freudenberg and Ahlhaus, *Monatsh.*, 1956, **87**, 1.
[10] (*a*) Shinoda and Sato, *J. Pharm. Soc. Japan*, 1928, **48**, No. 558, 109; 1928, **48**, No. 560, 117; (*b*) 1929, **49**, No. 563, 5; (*c*) 1931, **51**, 78; Shinoda and Kamagoye, 1928, **48**, No. 560, 119; Shinoda, Kamagoye, and Sato, 1931, **51**, 23; Shinoda, Sato, and Kamagoye, 1929, **49**, No. 571, 123; Fujise and Mitui, *Bull. Chem. Soc. Japan*, 1934, **9**, 24; Huzise and Tatsita, *Ber.*, 1941, **74**, 275.
[11] Robertson, Whalley, and Yates, *J.*, 1950, 3119.
[12] Anand, Gupta, Pankajamani, and Seshadri, *J. Sci. Ind. Res. India*, 1956, **15**, *B*, 263.

hydride reduction. 3 : 4 : 2′-Trihydroxychalcone was prepared by the condensation of 3 : 4-dihydroxyacetophenone [6] and salicylaldehyde in strongly alkaline solution. Methylation of 3′ : 4′-dihydroxyflavan gave 3′ : 4′-dimethoxyflavan, which was also synthesised from the available 2′-benzyloxy-αβ-dihydro-3 : 4-dimethoxychalcone.[13] The attempted preparation of 5 : 7 : 3′ : 4′-tetrahydroxy-6 : 8-dimethylflavan by Simonis synthesis from *CC*-dimethylphloroglucinol [14] and caffeyl chloride dibenzoate, followed by Clemmensen reduction, afforded crystals of the flavan which immediately resinified on exposure to air. Similar difficulty in the isolation of certain flavans has already been described.[15]

Experimental

General Procedure.—Solutions were concentrated in nitrogen under reduced pressure at <35°. Ferric chloride colours refer to reaction in ethanol.

Manometry.—Use was made of Haldane's constant-pressure respirometer,[16] in which the reaction vessel was connected by small-bore pressure tubing to a gas-burette, and to a constant-pressure manometer, the other limb of which was connected to a compensation vessel. *n*-Butyl phthalate was used in the manometer and in the gas-burette. Both vessels, immersed in a thermostat at 35°, were shaken at a speed sufficient to maintain the reaction mixture as a foam. A small tube containing the flavan, and attached to a glass fibre, was placed upright in the reaction vessel, surrounded by phosphate buffer. In this way the system could be equilibrated before the reaction commenced by dislodging the tube and shaking the contents. A solution of 0·1 mmole of flavan in 10 ml. of phosphate buffer (pH 8), or phosphate buffer–methanol (1 : 1) (10 ml.) was used. The progress of the reaction was followed by direct reading of the volume of the system on the gas burette, the movable limb of which was first adjusted so as to bring the liquid in both arms of the constant-pressure manometer to the same level. When absorption of oxygen ceased, no flavan could be detected in the paper chromatogram of the reaction mixture. After acidification of the mixture, the polymer was adsorbed on a column (10 × 1·2 cm.) of alumina, prepared in 2N-sulphuric acid. Potassium iodide (1 g.) was added to the sulphuric acid eluate which was set aside (15 min.) in the dark, and the liberated iodine was estimated with 0·01N-sodium thiosulphate. In another experiment, the oxidising agent was shown to be hydrogen peroxide, as the distillate gave a positive reaction with titanic sulphate and was indistinguishable from distilled water between 300—700 mμ.

Spectrophotometric Experiments and Analytical Samples.—A solution of the flavan (1 mmole) in phosphate buffer (pH 8; 100 ml.) or its equivalent of phosphate buffer–methanol (1 : 1) was shaken with oxygen until no more was absorbed. Samples were then withdrawn for spectrophotometric examination of the polymer, the solution being diluted where required with more phosphate buffer. For the isolation of the pure polymer phosphate ion was removed by introducing the reaction mixture into the middle compartment of an electrodialysis cell, constructed from "Pyrex" pipe-line,[17] and fitted with a "Permaplex" A-10 anion-exchange membrane, and a "Permaplex" C-10 cation-exchange membrane. The cell was supplied with D.C. at 100 v until the resistance approached a limit (*ca.* 10 hr.); the solution was then free from phosphate ion (molybdenum-blue test). Removal of phosphate ion caused precipitation of the polymer which was removed in the centrifuge, and dried (3 days at 20°/0·01 mm., followed by 8 hr. at 70°/0·01 mm. over P_2O_5). All the polymers were ashless on combustion.

Vanillin reaction. A 10% (w/v) ethanolic solution of vanillin was mixed with 12N-hydrochloric acid (2 : 1 v/v) and the freshly prepared reagent was employed at room temperature.

5 : 7-*Dihydroxyflavan.*—This had m. p. 196° (Found : C, 74·2; H, 5·9. Calc. for $C_{15}H_{14}O_3$: C, 74·4; H, 5·8%) when prepared by the method of Robertson, Whalley, and Yates.[11]

5 : 7-*Di*-O-*methyl*-(+)-*catechin.*—Aqueous 4M-sodium metaborate (10 ml.), methyl sulphate (2 ml.), and 2·5N-sodium hydroxide (8 ml.) were shaken with an ethanolic solution of (+)-catechin (2·9 g.) for 15 min.; the reaction mixture was then poured into ice-water and extracted with ether. The acidified aqueous phase was extracted with ether (4 × 100 ml.), and the

[13] Freudenberg, *Annalen*, 1925, **441**, 179.
[14] Robertson and Whalley, *J.*, 1951, 3355.
[15] Robertson, Venkateswarlu, and Whalley, *J.*, 1954, 3137.
[16] Haldane, *J. Path. Bact.*, 1921, **23**, 443; Dixon, "Manometric Methods," University Press, Cambridge, 1934, p. 6.
[17] Lovering and Smith, *Chem. and Ind.*, 1946, **24**, 298.

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ether phase was washed free from mineral acid and dried. Evaporation of the solvent ($MgSO_4$) left 5 : 7-*di*-O-*methyl*-(+)-*catechin* (2·6 g.), forming needles (from aqueous ethanol), m. p. 218—219°, $[\alpha]_D^{20}$ −1·0 (*c*, 1·1 in acetone; *l*, 1) {(+)-catechin, $[\alpha]_D^{20}$ +12° (*c*, 1·7); 5 : 7 : 3′ : 4′-tetra-*O*-methyl-(+)-catechin $[\alpha]_D^{20}$ −2° (*c*, 1·0)} (Found : C, 64·0; H, 5·6; OMe, 19·1. $C_{17}H_{18}O_6$ requires C, 64·0; H, 5·6; OMe, 19·1%). 5 : 7-Di-*O*-methyl-(+)-catechin gave a green ferric reaction, and a positive vanillin reaction.

5 : 7-*Dihydroxy*-3′ : 4′-*dimethoxyflavan*.—5 : 7-Dihydroxy-3′ : 4′-dimethoxyflavanone, m. p. 202° (Found : C, 64·9; H, 5·2; OMe, 19·7. Calc. for $C_{17}H_{16}O_6$: C, 64·6; H, 5·1; OMe, 19·5%), was prepared in 25% yield by an improvement of Shinoda and Sato's [10b] method. Reduction of the flavanone by Robertson, Whalley, and Yates's method [11] gave 5 : 7-*dihydroxy*-3′ : 4′-*dimethoxyflavan*, nodules (from xylene), m. p. 260° (Found : C, 67·3; H, 5·9. $C_{17}H_{18}O_5$ requires C, 67·5; H, 5·9%), which gave a positive vanillin reaction but no ferric reaction.

5 : 7 : 3′ : 4′-*Tetrahydroxyflavan*.—Eriodictyol, m. p. 267° (Found : C, 62·0; H, 4·0. Calc. for $C_{15}H_{12}O_6$: C, 62·5; H, 4·2%), was prepared in 20% yield (cf. Shinoda and Sato [10b]) by the method used for its 3′ : 4′-dimethyl ether. Reduction of eriodictyol by the method used for the 3′ : 4′-dimethyl ether gave the *flavan* which formed felted needles, m. p. 185° (from water) (Found : C, 62·1; H, 5·4. $C_{15}H_{14}O_5,H_2O$ requires C, 61·8; H, 5·5%), which were dried (P_2O_5) at 70°/0·1 mm. for 3 hr., and gave a green ferric reaction and a vanillin reaction.

3′ : 4′-*Dihydroxyflavan* (with Dr. W. E. Elstow [18]).—A mixture of an ethanolic solution (60 ml.) of 3 : 4-dihydroxyacetophenone [6] (19 g.) and salicylaldehyde (16 g.) and 40% (w/v) potassium hydroxide solution (150 ml.) was kept under nitrogen for 1 week. 3 : 4 : 2′-*Trihydroxychalcone* formed brown needles (30 g.) (from aqueous ethanol), m. p. 189° (Found : C, 70·3; H, 4·8. $C_{15}H_{12}O_4$ requires C, 70·3; H, 4·7%). An ethanolic solution of the chalcone (25·6 g.) was hydrogenated at 20°/1 atm. in the presence of Adams's platinic oxide catalyst (200 mg.), until hydrogen absorption (Found : 2·35 l.; Calc. : 2·30 l.) was complete. Evaporation of the filtrate left crude αβ-dihydro-3 : 4 : 2′-trihydroxychalcone which was benzoylated by the Schotten–Baumann method. 3 : 4 : 2′-*Tribenzoyloxy*-αβ-*dihydrochalcone* formed needles (55 g.) (from ethanol), m. p. 113° (Found : C, 75·6; H, 4·7. $C_{36}H_{26}O_7$ requires C, 75·8; H, 4·6%). Lithium aluminium hydride reduction of the dihydrochalcone (5·7 g.) gave 3′ : 4′-*dihydroxyflavan* which formed needles (2·6 g.) (from light petroleum [b. p. 60—80°]), m. p. 132° (Found : C, 74·4; H, 5·9. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%). The flavan gave a green ferric reaction.

3′ : 4′-*Dimethoxyflavan*.—Treatment at 0° of an ethereal solution of 3′ : 4′-dihydroxyflavan (2·6 g.) with ethereal diazomethane (*ca.* 2·8 g.) gave 3′ : 4′-*dimethoxyflavan* as thick lamellæ (2·6 g.), m. p. 99—100° (Found : C, 75·9; H, 6·5. $C_{17}H_{18}O_3$ requires C, 75·7; H, 6·7%), undepressed by another specimen, m. p. 99—100°, prepared by lithium aluminium hydride reduction of the corresponding 2′-benzoyloxy-αβ-dihydro-3 : 4-dimethoxychalcone.[13]

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British Leather Manufacturers' Research Association,
Milton Park, Egham, Surrey.

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[18] Elstow, Ph.D. Thesis, London University, 1954.

301. *Activity Coefficients of Nitric and Perchloric Acids in Dilute Aqueous Solution from E.M.F. and Transport-number Measurements.*

By A. K. Covington and J. E. Prue.

Precise values have been obtained for the activity coefficients of nitric and perchloric acids in aqueous solutions at 25° up to 0·1M by combining measurements on cells with transport-number measurements. The e.m.f. measurements were made by our recently developed glass-electrode technique and the transport numbers were obtained by the moving-boundary method. The activity coefficients are compared with those of other strong acids.

There are no precise values for the activity coefficients γ of nitric and perchloric acids in dilute aqueous solution. The hydrogen electrode cannot be used because of its reducing action and there is a lack of suitable anion-reversible electrodes. However, a technique has recently been developed [1, 2] by which it is possible to obtain results with glass electrodes comparable in precision with those obtained in the most exact work with "classical" electrodes, and we have now used it with nitric and perchloric acids. Measurements on concentration cells of the type:

$$\text{Glass electrode}|HNO_3(m_1)|HNO_3(m_2)|\text{glass electrode}$$

have been combined with transport numbers t^+, t^- obtained by the moving-boundary method. The measurements of e.m.f. of concentration cells were made as previously described for hydrochloric acid.[2] Transport numbers of high accuracy were required and the performance of the apparatus was tested by repeating the measurements of Longsworth [3] on hydrochloric acid.

Experimental

Materials.—"AnalaR" concentrated nitric acid (shown to be free from oxides of nitrogen) and perchloric acid were used without further purification. Solutions were prepared with conductivity water from an ion-exchange column and standardised by weight-titration through sodium borate solution against constant-boiling hydrochloric acid. Conversions from molality to molarity scales were made by using the following equations applicable up to 0·1M:

$$\rho(HNO_3) = 0{\cdot}99707 + 0{\cdot}0332m \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\rho(HClO_4) = 0{\cdot}99707 + 0{\cdot}0573m \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The equations are based on densities (ρ) obtained with a 15 ml. Ostwald pycnometer at 25°. The silver and cadmium used were spectroscopically pure rods supplied by Messrs. Johnson, Matthey and Co., Ltd.

Apparatus.—The moving-boundary measurements were made with an autogenic boundary rising from a cadmium anode in the case of hydrochloric acid and a silver anode in the case of nitric and perchloric acids. Stable boundaries could not be obtained with nitric and perchloric acids with a cadmium anode, and with nitric acid a white solid was deposited on the metal surface. A very small amount of a black sludge was formed at the silver anode, but *X*-ray powder photographs showed that this contained no significant amount of anything other than metallic silver. The anode was cemented into the moving-boundary cell with "Araldite" which is unattacked by hydrochloric acid and only slightly coloured by the oxidising acids. The cell was based on Le Roy and Gordon's design.[4] The graduated tubes were of 3·5 and 3·0

[1] Covington and Prue, *J.*, 1955, 3696.
[2] Covington and Prue, *J.*, 1955, 3701.
[3] Longsworth, *J. Amer. Chem. Soc.*, 1932, **54**, 2741.
[4] Le Roy and Gordon, *J. Chem. Phys.*, 1938, **6**, 398.

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mm. bore graduated every 0·5 cm. over a 20 cm. length; the graduation marks extended on either side of the tube leaving a clear space at front and back, so that the boundary was never obscured by a graduation mark. The method of weighing of mercury was used to calibrate the tube by volume over 10 cm. lengths at 1 cm. intervals. A cathetometer (Precision Tool and Instrument Co.) which could be read to 0·001 cm. was used for measuring the length of the mercury thread. The moving boundary was observed with a system of the kind described by MacInnes, Cowperthwaite, and Huang,[5] the cell being placed in a water thermostat (at 25·00° ± 0·01°) with two glass sides. The motion of the boundary was timed with a " split-second " stop-watch having two second-hands, one of which can be stopped and, after the time has been read, resynchronised with the other hand. The watch was checked against standard time and its error found to be negligible.

One of the major difficulties of the moving-boundary method is to maintain a constant current during the electrolysis, since there is a steady change of resistance during an experiment. We required a mains-operated device which would supply a current of between 0·5 and 2·5 mA constant to 0·2% through a load whose resistance changed tenfold in the range 5000—500,000 ohm. The only previous accurate measurements on acid solutions are those of Longsworth[3] who used an elaborate mechanical device. Other workers[4, 6] who have used electronic techniques have only had to contend with changes of 50—100% in the resistance. A satisfactory mains-operated constant-current device was, however, devised and is described elsewhere.[7] After a " warming-up " period on a dummy load, the current was switched to the moving-boundary cell with a double ceramic switch of the " make-before-break " type. Up to 500 v were available for the cell. The current was measured by determining the potential drop across a 100 ohm manganin-wound standard resistance (certified by the N.P.L.) with a vernier potentiometer. The usual precautions in making accurate potentiometric measurements were taken and the positive pole was grounded so that the potentiometer circuit should be near ground potential and the possible effects of electrical leakage minimised.

Procedure.—The moving-boundary cell was rinsed three times with solution and filled through a drawn-out capillary tube. The cell was kept for 1 hr. in the thermostat before the run was started. The motion of the boundary was timed over at least 15 cm. of the tube, time readings being taken at every 5 mm. graduation mark and current readings every 2 mm.

Results and Discussion

Transport Numbers.—From a plot of current i against time t, the mean value of the current while the boundary was traversing each 5 mm. length between graduations was estimated. Values of the product $i\delta t$ over the same interval were summed over 10 cm. sections of the tube. Some typical values obtained during a run with perchloric acid are given in column 3 of Table 1. Column 4 contains corresponding values of $cF\Delta V$ where c

Table 1.

$[HClO_4] = 0{\cdot}01925_7$ mole l.$^{-1}$. Temp. 25°. $i = 1{\cdot}0131 \pm 0{\cdot}0003$ mA.

Δx (mm.)	ΔV (ml.)	$\Sigma\, i\delta t$ (10^{-3}c)	$cF\Delta V$ (10^{-3}c)	$t^+_{obs.}$
0—100	0·6925	1522·1	1286·7	0·8453
10—110	0·6944	1525·6	1290·3	0·8458
20—120	0·6954	1527·1	1292·1	0·8461
30—130	0·6967	1530·4	1294·5	0·8459
40—140	0·6976	1531·9	1296·2	0·8461
50—150	0·6984	1534·6	1297·7	0·8456
60—160	0·6995	1536·7	1299·7	0·8458
80—180	0·7002	1538·9	1301·0	0·8454
			Mean =	$0{\cdot}8457_6$
			Mean of 17 values =	0·8457

is the concentration of the acid solution, F is the faraday (taken as 96,488 c mole^{-1}) and ΔV is the volume swept through. The ratio of the figures in column 4 to those in column 3 gives values of $t^+_{obs.}$. A mean value was calculated from not less than 11 values in each

[5] MacInnes, Cowperthwaite, and Huang, *J. Amer. Chem. Soc.*, 1927, **49**, 1710.
[6] Hartley and Donaldson, *Trans. Faraday Soc.*, 1937, **33**, 457.
[7] Hopkins and Covington, *J. Sci. Instr.*, 1957, **34**, 20.

experiment. The standard deviation for the mean was 0·0001 throughout except for the first entry in Table 2, where it was 0·0002.

A volume correction was applied to the transport numbers to allow for the change in volume behind the boundary at the anode. These small corrections (see Tables 2, 3, and 4) were estimated from partial molal volumes calculated from density data given by International Critical Tables ($CdCl_2$, HNO_3), Longsworth [3] (Cd, Ag, $AgNO_3$), Wirth [8] (HCl), Mazzuchelli and Rossi [9] ($AgClO_4$), and Bigeleisen [10] ($HClO_4$). Because the specific

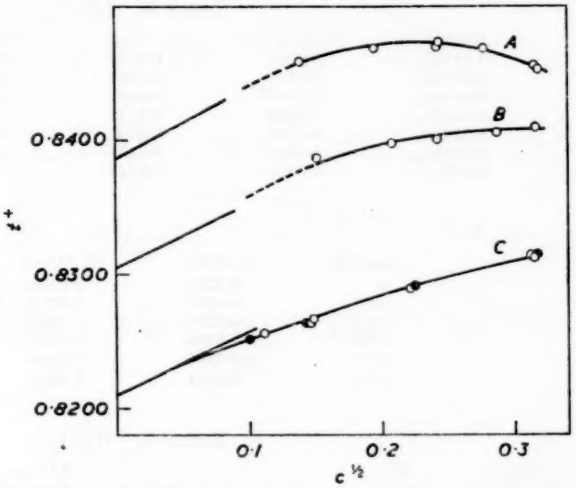

FIG. 1. *A*, $HClO_4$; *B*, HNO_3; *C*, HCl.

conductivity of the water used was less than 10^{-7} ohm^{-1} cm.$^{-1}$, no solvent correction was necessary.

The results obtained are given in Tables 2, 3, and 4 and plotted in Fig. 1. The reproducibility of the runs was about 0·0002 in t^+, and we do not believe that the measure-

TABLE 2. HCl.

c (mole l.$^{-1}$)	$c^{\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ l.$^{-\frac{1}{2}}$)	$t^+_{obs.}$	Vol. corr.	$t^+_{corr.}$
0·01231 *	0·1110	0·8255	0·0001	0·8256
0·02144$_7$	0·1464	0·8263	0·0002	0·8265
0·02181 *	0·1477	0·8264	0·0002	0·8266
0·04886 *	0·2210	0·8284	0·0005	0·8289
0·09710$_4$	0·3116	0·8305	0·0009	0·8314
0·09899 *	0·3146	0·8303	0·0009	0·8312

* Obtained with the less satisfactory constant-current device of Bender and Lewis (*J. Chem. Educ.*, 1947, **24**, 454).

TABLE 3. HNO_3.

c (mole l.$^{-1}$)	$c^{\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ l.$^{-\frac{1}{2}}$)	$t^+_{obs.}$	Vol. corr.	$t^+_{corr.}$
0·02297$_5$	0·1515	0·8385	0·0001	0·8386
0·04306$_9$	0·2075	0·8395	0·0002	0·8397
0·05841$_4$	0·2417	0·8396	0·0004	0·8400
0·08205$_3$	0·2864	0·8400	0·0005	0·8405
0·1002$_2$	0·3163	0·8403	0·0006	0·8409

ments of time, volume, current, or concentration can lead to a systematic error greater than 0·0003 in t^+. The results for hydrochloric acid are in good agreement with those of Longsworth [3] (full circles, ●, in Fig. 1).

[8] Wirth, *J. Amer. Chem. Soc.*, 1940, **62**, 1128.
[9] Mazzuchelli and Rossi, *Gazzetta*, 1927, **57**, 383.
[10] Bigeleisen, *J. Phys. Chem.*, 1947, **51**, 1369.

In Fig. 1 the Onsager theoretical limiting-law slopes have been drawn, the intercepts on the ordinate corresponding to values of the transport numbers at infinite dilution obtained from limiting equivalent conductivities.[11] The results for nitric and perchloric acids approach the limiting slope from above. In this, they resemble nitrates [12, 13] rather than most uni-univalent electrolytes.[13] Values of the transport numbers at rounded concentrations interpolated from a large-scale plot are given in Table 5.

TABLE 4. $HClO_4$.

c (mole l.$^{-1}$)	$c^{\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ l.$^{-\frac{1}{2}}$)	$t^+_{obs.}$	Vol. corr.	$t^+_{corr.}$
$0{\cdot}01925_7$	0·1388	0·8457	0·0001	0·8458
$0{\cdot}03785_0$	0·1945	0·8467	0·0001	0·8468
$0{\cdot}05840_9$	0·2417	0·8467	0·0002	0·8469
$0{\cdot}05905_2$	0·2430	0·8471	0·0002	0·8473
$0{\cdot}07649_0$	0·2766	0·8465	0·0003	0·8468
$0{\cdot}09933_3$	0·3152	0·8451	0·0004	0·8455
$0{\cdot}1011_2$	0·3180	0·8448	0·0004	0·8452

TABLE 5.

c (mole/l.)	t^+ (HCl)	t^+ (HNO_3)	t^+ ($HClO_4$)
0	0·8210	0·8304	0·8386
0·02	0·8265	0·8377	0·8456
0·04	0·8284	0·8394	0·8471
0·06	0·8296	0·8402	0·8473
0·08	0·8306	0·8406	0·8466
0·10	0·8314	0·8408	0·8452

TABLE 6. HNO_3.

$10^3 m_2$ (mole kg.$^{-1}$)	E (mv)	t^-	$-\Delta \log \gamma$	$\Delta \log \gamma - -\Delta \log (\gamma^{st})^{2\cdot5}$	$\Delta \log \gamma - -\Delta \log (\gamma^{st})^{3\cdot0}$	Δm (mole kg.$^{-1}$)
6·599	$20{\cdot}77_3$	0·1656	0·06046	−0·00709	−0·01293	0·08540
9·546	17·76	0·1645	0·05460	−0·00682	−0·01227	0·08245
14·28	14·50	0·1633	0·04776	−0·00684	−0·01174	0·07772
21·89	11·10	0·1621	0·03890	−0·00611	−0·01026	0·07011
23·19	10·61	0·1619	0·03945	−0·00782	−0·01185	0·06881
28·89	8·90	0·1614	0·03345	−0·00639	−0·00994	0·06311
44·53	$5{\cdot}50_3$	0·1603	0·02390	−0·00643	−0·00885	0·04747
48·95	$4{\cdot}79_5$	0·1602	0·02025	−0·00497	−0·00712	0·04305
64·93	2·64	0·1596	0·01143	−0·00287	−0·00411	0·02707
80·13	1·05	0·1594	0·00431	−0·00088	−0·00139	0·01187
92·00	0	0·1592	0	0	0	0

Cell e.m.f.'s and Activity Coefficients.—The extrapolations necessary to eliminate the effects of asymmetry potentials were similar to those previously used for hydrochloric acid.[2] The results were analysed in the same way, except that a standard value, γ^{st}, of the activity coefficient was defined by

$$\log \gamma^{st(\sigma)} = -Am^{\frac{1}{2}}/(1 + \sigma m^{\frac{1}{2}}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where the factor σ was not set equal to unity as with hydrochloric acid. If σ is set equal to unity, then plots of $\Delta \log \gamma - \Delta \log \gamma^{st}$ against Δm are not linear. This is not surprising since the nitrate and perchlorate ions are large and according to the Debye–Hückel theory $\sigma = a/a^\circ$ where a is the closest distance of approach of ions and a° is a constant with the value 3·04 Å at 25°. The results obtained by using values of $\sigma = 2{\cdot}5$, 3·0 are shown in Tables 6 and 7. The corresponding plots in Figs. 2 and 3 show that the fit in both cases is slightly better for $\sigma = 3{\cdot}0$ but, except for one nitric acid point, the

[11] Robinson and Stokes, "Electrolyte Solutions," Butterworths 1955, p. 452.
[12] MacInnes and Longsworth, *Chem. Rev.*, 1932, **11**, 171.
[13] Longsworth, *J. Amer. Chem. Soc.*, 1935, **57**, 1185.

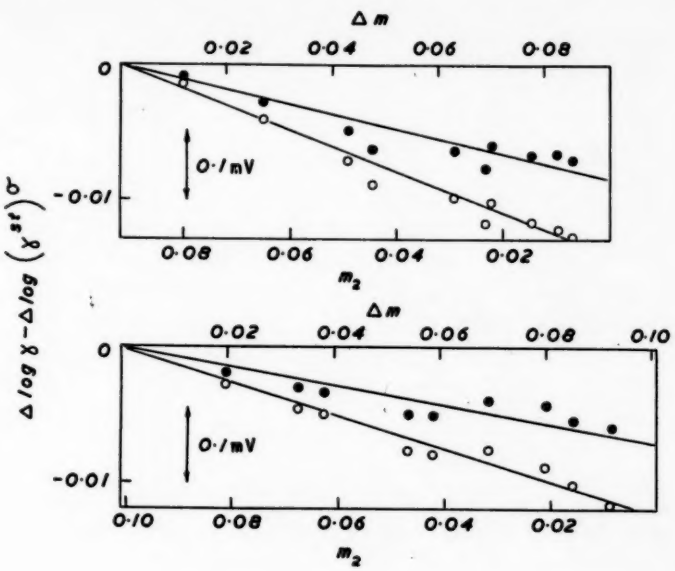

FIG. 2. ●, $\sigma = 2{\cdot}5$; ○, $\sigma = 3{\cdot}0$.

FIG. 3. ●, $\sigma = 2{\cdot}5$; ○, $\sigma = 3{\cdot}0$.

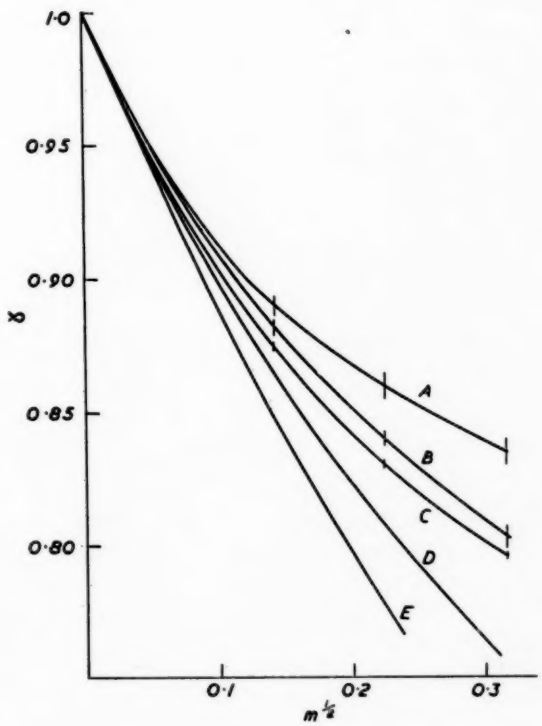

FIG. 4. *A*, HI; *B*, HBr, HNO_3, $HClO_4$; *C*, HCl; *D*, $\sigma = 1$, $B' = 0$; *E*, limiting law.

TABLE 7. $HClO_4$.

10^3m_2 (mole kg.$^{-1}$)	E (mv)	t^-	$-\Delta \log \gamma$	$\Delta \log \gamma$ $-\Delta \log (\gamma^m)^{2\cdot5}$	$\Delta \log \gamma$ $-\Delta \log (\gamma^{t-})^{2\cdot0}$	Δm (mole kg.$^{-1}$)
8·390	18·66	0·1570	0·05803	−0·00589	−0·01185	0·09253
15·50	13·93$_5$	0·1553	0·04676	−0·00529	−0·01016	0·08540
20·77	11·72	0·1544	0·04038	−0·00423	−0·00884	0·08013
31·60	8·57	0·1534	0·03130	−0·00386	−0·00755	0·06930
42·43	6·35	0·1528	0·02590	−0·00501	−0·00793	0·05847
47·00	5·59	0·1528	0·02346	−0·00493	−0·00755	0·05390
62·55	3·50	0·1528	0·01505	−0·00327	−0·00500	0·03835
67·13	2·98	0·1529	0·01309	−0·00302	−0·00451	0·03377
81·06	1·60	0·1535	0·00734	−0·00189	−0·00272	0·01984
100·9	0	0·1548	0	0	0	0

deviations from the straight lines are always less than 0·03 mv. The straight lines drawn correspond to the values

HNO_3 (i) $\sigma = 2{\cdot}5$, $B' = -0{\cdot}092$; (ii) $\sigma = 3{\cdot}0$, $B' = -0{\cdot}154$
$HClO_4$ (i) $\sigma = 2{\cdot}5$, $B' = -0{\cdot}070$; (ii) $\sigma = 3{\cdot}0$, $B' = -0{\cdot}123$

in the equation

$$\log \gamma = -Am^{\frac{1}{2}}/(1 + \sigma m^{\frac{1}{2}}) + B'm \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Values of γ corresponding to the alternative values of the parameters in equation (4) are given in Table 8. They would be changed by 0·001 or 0·002 by a systematic error of 0·0003 in the transport numbers. The concentration-cell results which Stonehill [14] obtained for nitric acid with the quinhydrone electrode when analysed with our transport-number data are found to be in approximate agreement with our own.

The smoothed values of the activity coefficients of nitric and perchloric acids are compared in Table 8 with those obtained by other workers for hydrochloric, hydrobromic, and hydriodic acid. In the cases of hydrochloric and hydrobromic acids the γ values are

TABLE 8.

m (mole kg.$^{-1}$)	HCl [a]	HBr [b]	HNO_3 (i)	HNO_3 (ii)	$HClO_4$ (i)	$HClO_4$ (ii)	HI [c]
0·01	0·904	0·906	0·909	0·911	0·909	0·911	0·91
0·02	0·875	0·879	0·881	0·884	0·882	0·885	0·89
0·05	0·830	0·838	0·838	0·840	0·841	0·843	0·86
0·10	0·796	0·805	0·796	0·798	0·800	0·804	0·83$_5$

[a] Hills and Ives, *J.*, 1951, 318. [b] Harned, Keston, and Donelson, *J. Amer. Chem. Soc.*, 1936, **58**, 989. [c] Calc. from Pearce and Fortsch, *ibid.*, 1923, **45**, 2852.

also uncertain by 0·002 to 0·003 according to the smoothing function used and the weighting of the points for the most dilute solutions. The activity coefficients are plotted in Fig. 4, the values from different smoothing formulæ and the possible errors being shown by the vertical bars on the Figure. The limiting-law curve and the curve corresponding to $\sigma = 1$, $B' = 0$ are also shown. We see that the activity coefficients of hydrobromic, nitric, and perchloric acids are very similar and lie in a sheaf together above those of hydrochloric acid. We note that as the size of the anion increases the standard activity equation with $\sigma = 1$, $B' = 0$ becomes increasingly unsatisfactory; we saw earlier that in the cases of nitric and perchloric acids the deviations from it cannot be represented by the addition of a linear term in m.

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READING UNIVERSITY. [*Received, October 24th*, 1956.]

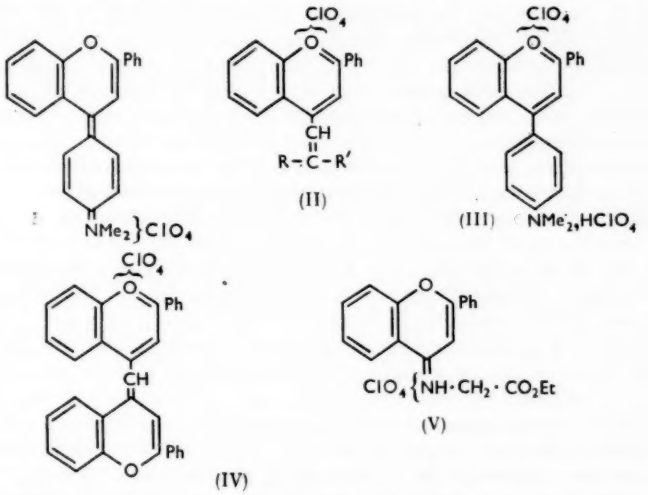
[14] Stonehill, *J.*, 1943, 647.

302. *Reactions of Flavylium Salts with Dimethylaniline and Malonic Acid.*

By M. Blackburn, G. B. Sankey, Alexander Robertson, and W. B. Whalley.

The nature and scope of the condensation of selected flavylium salts with dimethylaniline and with malonic acid have been investigated.

The condensation of dimethylaniline, diarylethylenes, and malonic acid with flavylium perchlorate in hot acetic acid to yield products of type (I), (II), and (IV) respectively has been recorded by Wizinger [1] who in collaboration with Luthiger [2] subsequently examined the formation of compounds (I) and (II) in some detail. This kind of condensation appeared to us to be of some significance in connexion with the structure of dracorubin [3] and possible synthetical routes to this type of molecule, more especially because for some



time we have envisaged the phytochemical production of the dracorubin molecule to be essentially an oxidative coupling of the appropriate benzopyrylium salt (or base) with a flavan, or their equivalents. Accordingly the present investigation was initiated to determine the scope and nature of this coupling reaction exhibited by flavylium perchlorate, including the effects of substituents in the flavylium residue.

Thus, in agreement with the structure of the condensation products proposed by Wizinger and Luthiger,[2] flavylium salts with a substituent in the 4-position fail to react with dimethylaniline. With 3- or 5-substituted flavylium salts, *e.g.*, 3-methoxy-, 7-hydroxy-3-methoxy-, 3-phenyl-, 5 : 7-dimethyl-, and 5 : 7-dimethoxy-flavylium perchlorate the reaction was extremely slow and, although the mixture became highly coloured as in successful cases, only the starting materials could be isolated. On the other hand 7-hydroxy-, 7-methoxy-, 4′-hydroxy-, 4′-methoxy-, 6 : 7-dimethoxy-, and 7 : 4′-dihydroxy-8-methoxy-flavylium perchlorate readily furnished the appropriate *p*-dimethylaminophenyl derivatives type (I) which have been characterised by the formation of salts. In agreement with structure (I) these products form a series of well-defined diperchlorates, of type (III), which, as would be expected on general grounds, are much paler than corresponding monoperchlorates.

[1] Wizinger, *Chimia (Switz.)*, 1952, **6**, 243.
[2] Wizinger and Luthiger, *Helv. Chim. Acta*, 1953, **36**, 526.
[3] Robertson, Whalley, and Yates, *J.*, 1950, 3117.

Attempts to obtain degradative evidence for structures of type (I) were unsuccessful; *e.g.*, 4-*p*-dimethylaminophenylflavylium perchlorate is not readily oxidised with ozone, and with potassium permanganate or chromic oxide furnished only benzoic acid; degradation with alkali gave dimethylaniline and acetophenone.

The scope of the condensation of flavylium salts with malonic acid, recorded by Wizinger [1] without experimental details, to give 4-4′-flavenylidenemethylflavylium perchlorates of type (IV) has been found to follow closely the behaviour with dimethylaniline. We are indebted to Professor Wizinger for providing us with the details of his unpublished experimental conditions, *viz.*, the interaction of the components in acetic acid containing sodium acetate. This implies that the flavylium base is the active component and we have found that this reaction and also that with dimethylaniline is an oxidative coupling depending on the supply of atmospheric oxygen. The reaction does not take place in nitrogen, and, further, the condensation is equally productive when flavylium salts containing non-oxidising anions (*e.g.*, chloride) are employed.

Attempts to substantiate, by degradation, the 4-4′-flavenylidenemethylflavylium salt structure allocated to (IV) were unsuccessful; *e.g.*, ozonolysis gave only salicyclic acid and fusion with alkali yielded benzoic acid. The exceptional stability to oxidation and alkali-fission encountered in these compounds, together with their intense colours, may be ascribed to the distribution of the cationic charge over the whole cation as in the case of the cyanine and triphenylmethane dyes.

The possibility that the observations described in this paper have biological significance has already been mentioned. The natural anthocyanidin pigments possess substituents in the 3- and the 5-position, and yet in the closely analogous and almost certainly biogenetically related natural flavones and flavanones there are several which do not have substituents in these positions, *e.g.*, flavone, 7-hydroxy-4′-methoxyflavone (pratol), 7 : 3′ : 4′-trihydroxy- (butin), and 7 : 4′-dihydroxy-flavanone (liquiritegenin). This discrepancy may well be due in some measure to the reactivity towards " formyl equivalents " which 3- and 5-unsubstituted flavylium salts clearly exhibit and thus their existence in plant tissues might be transitory. Whilst malonic acid seldom occurs in plant tissues and is an inhibitor of the tricarboxylic acid cycle, its role in the condensations described is clearly the provision of one carbon atom, *i.e.*, the " formyl equivalent." It might be expected that the biological processes responsible for the frequent provision of one carbon atom fragments in phytochemical processes could function in this role. In this connexion it may be noted that the brief report [4] of the oxidative coupling of flavylium perchlorate and glycine ethyl ester to furnish compound (V) is a further example and extension of the reactions now discussed.

Experimental

Several of the picrates and perchlorates, especially the diperchlorates, melt with violent decomposition and consequently analyses have been difficult or impossible in some cases. Salts which have not been analysed for this reason are marked with an asterisk.

4-p-*Dimethylaminophenyl-2-phenylbenzopyranol.*—A solution of flavylium perchlorate (1 g.) in methanol (13 ml.) containing dimethylaniline (0·5 g.), was refluxed for 90 min. On cooling, the intense blue mixture deposited 4-*p*-dimethylaminophenylflavylium perchlorate (0·3 g.) which separated from methanol in purple needes, m. p. 250° (decomp.), and from acetic acid in green plates, m. p. 250° (decomp.) (Found: C, 65·0; H, 4·8; N, 3·3; Cl, 8·6. Calc. for $C_{23}H_{20}O_5NCl$: C, 64·8; H, 4·8; N, 3·3; Cl, 8·2%) (Wizinger and Luthiger [2] give m. p. 254°). The same compound separated in green plates (0·5 g.), m. p. 250° (decomp.), when boiling methanol was replaced by boiling acetic acid. The colour of a warm solution of this perchlorate (2 g.) in methanol (20 ml.) was discharged by the drop-wise addition of 2N-aqueous sodium hydroxide. Purification of the crystalline product (1·5 g.) from methanol furnished the *methyl ether* of 4-*p*-dimethylaminophenyl-2-phenylbenzopyranol in stout tablets, m. p. 118° (Found: C, 79·9; H, 6·3; N, 3·9; OMe, 8·4. $C_{24}H_{23}O_2N$ requires C, 80·7; H, 6·4; N, 3·9; OMe, 8·7%).

[4] Shriner, XIVth Internat. Congr. Pure Appl. Chem., Congress Handbook, 1955, p. 265.

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Addition of perchloric acid to a methanolic solution of this ether regenerated the parent perchlorate. Prepared in alcohol, the *picrate* separated from acetic acid containing 1% picric acid in golden-brown needles, m. p. 244° (decomp.) (Found: C, 63·1; H, 4·2; N, 9·8. $C_{29}H_{22}O_8N_4$ requires C, 62·8; H, 4·0; N, 10·1%). The *ferrichloride* separated from acetic acid in purple plates, m. p. 149° (decomp.) (Found: C, 52·9; H, 3·9; N, 2·6; Fe, 10·2. $C_{23}H_{20}ONCl_4Fe$ requires C, 52·7; H, 3·8; N, 2·7; Fe, 10·7%). A solution of 4-*p*-dimethylaminophenylflavylium perchlorate (0·1 g.) in 60% perchloric acid (3 ml.) slowly deposited the *diperchlorate* (0·1 g.) in bright yellow plates, m. p. 100—170° (violent decomp.) (Found: N, 2·6. $C_{23}H_{21}O_9NCl_2$ requires N, 2·7%). Diluted with water a solution of this salt became purple owing to the regeneration of the monoperchlorate.

Dimethylaniline reacted with 4′-methoxyflavylium perchlorate to yield green needles, m. p. 134° (decomp.), of 4-p-*dimethylaminophenyl-4′-methoxyflavylium perchlorate* (Found: C, 60·7; H, 5·4; N, 2·6. $C_{24}H_{22}O_6NCl,H_2O$ requires C, 60·9; H, 5·1; N, 3·0%) which gave a diperchlorate* in orange needles, m. p. 120—140° (decomp.). The *picrate* separated from acetic acid in golden-brown needles, m. p. 226° (decomp.) (Found: N, 9·6. $C_{30}H_{24}O_9N_4$ requires N, 9·6%).

7-Hydroxyflavylium perchlorate gave 4-p-*dimethylaminophenyl-7-hydroxyflavylium perchlorate* in dark green needles, m. p. 273° (decomp.) (Found: Cl, 8·8. $C_{23}H_{20}O_6NCl$ requires Cl, 7·9%). The *diperchlorate* formed yellow plates, m. p. 135—180° (decomp.) (Found: Cl, 14·6. $C_{23}H_{21}O_{10}NCl_2$ requires Cl, 13·1%), and the *picrate* golden needles, m. p. 250—260° (decomp.) (Found: C, 60·7; H, 3·9; N, 9·7. $C_{29}H_{22}O_9N_4$ requires C, 61·0; H, 4·0; N, 9·8%).

4-p-*Dimethylaminophenyl-4′-hydroxyflavylium perchlorate* formed dark green needles, m. p. 280° (decomp.) (Found: N, 3·0. $C_{23}H_{20}O_6NCl$ requires N, 3·1%), giving a diperchlorate* which separated from 60% perchloric acid in golden-yellow plates, m. p. 110—150° (decomp.). The *picrate* crystallised from acetic acid in chocolate-coloured prisms, m. p. 256° (decomp.) (Found: N, 9·6. $C_{29}H_{22}O_9N_4$ requires N, 9·8%).

4-p-*Dimethylaminophenyl-7-methoxyflavylium perchlorate* formed purple plates, m. p. 246—248° (decomp.), from acetic acid (Found: N, 3·0. $C_{24}H_{22}O_6NCl$ requires N, 3·1%); the *picrate* separated from alcohol in dark blue plates, m. p. 258° (decomp.) (Found: N, 10·3. $C_{30}H_{24}O_9N_4$ requires N, 9·6%).

7 : 4′-Dihydroxyflavylium perchlorate yielded dark green needles of 4-p-*dimethylaminophenyl-7 : 4′-dihydroxyflavylium perchlorate*, m. p. 350° (Found: N, 2·5. $C_{23}H_{20}O_7NCl$ requires N, 3·3%).

6 : 7-Dimethoxyflavylium perchlorate gave 4-p-*dimethylaminophenyl-6 : 7-dimethoxyflavylium perchlorate* in dark green needles, m. p. 286° (decomp.) (Found: N, 3·1. $C_{25}H_{24}O_7NCl$ requires N, 2·8%). The *picrate* formed bronze needles, m. p. 270° (decomp.) (Found: N, 10·0. $C_{31}H_{26}O_{10}N_4$ requires N, 9·4%).

Condensation of Flavylium Chloride and Dimethylaniline.—Flavylium chloride (1 g.) and dimethylaniline (0·5 g.) were heated in boiling methanol for 90 min. but, on cooling, the intense blue solution did not deposit a product. The mixture was treated with excess of methanolic sodium acetate followed by water (200 ml.), and a colourless semisolid precipitate was isolated with ether and treated with perchloric acid in acetic acid, giving the perchlorate of 4-*p*-dimethylaminophenylbenzopyranol, identical with an authentic specimen.

Attempts to effect this reaction in an atmosphere of nitrogen were unsuccessful and gave only very pale-blue reaction mixtures containing only the starting materials; admission of air at once produced the intense blue colour.

5 : 7-*Dimethylflavylium Perchlorate.*—Prepared by the condensation of 2-hydroxy-4 : 6-dimethylbenzaldehyde [5] and acetophenone according to standard practice, 5 : 7-*dimethylflavylium perchlorate* separated from acetic acid in yellow needles, m. p. 229° (decomp.) (Found: C, 60·7; H, 4·7. $C_{17}H_{13}O_5Cl$ requires C, 61·1; H, 4·5%).

6 : 7-*Dimethoxyflavylium perchlorate* was prepared from 2-hydroxy-4 : 5-dimethoxybenzaldehyde and acetophenone and separated from acetic acid in needles, m. p. 298° (decomp.) (Found: C, 54·6; H, 4·1. $C_{17}H_{15}O_7Cl$ requires C, 55·7; H, 4·1%).

Alkali-degradation of 4-p-*Dimethylaminophenylbenzopyranol.*—(*a*) When a solution of the perchlorate (1 g.) in methanol (15 ml.) containing 33% aqueous potassium hydroxide (10 ml.) was refluxed for 7½ hr. in a stream of nitrogen, and the effluent gas passed into aqueous 2 : 4-

[5] Gattermann, *Annalen*, 1907, **357**, 328.

XUM

dinitrophenylhydrazine sulphate, the hydrazone (10 mg.) of acetophenone was obtained in orange needles, m. p. 242°, after purification from alcohol. Separation of the hydrolysate into neutral, phenolic, and acidic components furnished acetophenone (20 mg.), identified as the 2 : 4-dinitrophenylhydrazone, as the only characterisable product.

(*b*) Fusion of the perchlorate (2 g.) with potassium hydroxide (6 g.) in water (5 ml.) in a stream of nitrogen at 320° during 30 min., followed by separation of the hydrolysate into neutral, acidic, and phenolic components, gave acetophenone, characterised as the 2 : 4-dinitrophenylhydrazone, and dimethylaniline characterised as the picrate.

Condensation of Flavylium Perchlorates with Malonic Acid.—Interaction of flavylium perchlorate (6·2 g.), malonic acid (1·04 g.), and sodium acetate (1·5 g.) in boiling acetic acid (150 ml.) for 20 min. or at room temperature for 12 hr. gave a crystalline product which on purification from acetic acid containing 1% of perchloric acid furnished 4-4′-*flavenylidenemethylflavylium perchlorate* (4 g.) in lustrous, green needles, m. p. 254° (decomp.) (Found : C, 70·0; H, 4·1; $C_{31}H_{21}O_6Cl$ requires C, 70·7; H, 4·0%). Wizinger [6] found m. p. 250—254°. Prepared by the addition of sodium hydroxide solution to a solution of the perchlorate in methanol, the *pyranol base* separated from light petroleum (b. p. 60—80°) in yellow needles, m. p. 148° (decomp.) (Found : C, 84·2; H, 5·5. $C_{31}H_{22}O_3$ requires C, 84·2; H, 5·0%). This compound was very unstable and the analysis had to be performed within a few hours of preparation. With perchloric acid it regenerated the perchlorate and with picric acid furnished the *picrate* in dark red needles, m. p. 270° (Found : N, 6·5. $C_{37}H_{23}O_9N_3$ requires N, 6·4%).

On being refluxed for 15 min. a solution of flavylium ferrichloride (2 g.), malonic acid (0·26 g.), and sodium acetate (0·41 g.) in acetic acid (25 ml.) gave the *ferrichloride*, which separated from acetic acid in dark blue plates, m. p. 256° (decomp.) (Found : C, 59·7; H, 3·6. $C_{31}H_{21}O_3FeCl_4$ requires C, 59·7; H, 3·4%). The free base from this had m. p. 148° and was identical with that obtained from the perchlorate.

The condensation of various flavylium perchlorates with malonic acid furnished analogous products as follows :

6-Hydroxyflavylium perchlorate (2 g.) gave 6-*hydroxy*-4-(6-*hydroxy*-4-*flavenylidenemethyl*)-*flavylium perchlorate* (0·9 g.) dark green needles (from acetic acid), m. p. 306° (decomp.) (Found : C, 66·4; H, 4·0. $C_{31}H_{21}O_8Cl$ requires C, 66·9; H, 3·8%).

7-Hydroxyflavylium perchlorate (1 g.) gave 7-*hydroxy*-4-(7-*hydroxy*-4-*flavenylidenemethyl*)-*flavylium perchlorate* (0·5 g.) in olive-green needles, m. p. 283° (decomp.) from acetic acid (Found : C, 67·0; H, 4·2%).

7-Methoxyflavylium perchlorate (1 g.) gave 7-*methoxy*-4-(7-*methoxy*-4-*flavenylidenemethyl*)-*flavylium perchlorate dihydrate* (0·5 g.) in dark green needles, m. p. 289° (decomp.) from acetic acid (Found : C, 63·5; H, 4·9. $C_{33}H_{25}O_8Cl,2H_2O$ requires C, 63·9; H, 4·7%).

8-Methoxyflavylium perchlorate (1 g.) furnished 8-*methoxy*-4-(8-*methoxy*-4-*flavenylidenemethyl*)*flavylium perchlorate dihydrate* (0·48 g.) in plates, m. p. 296° (decomp.), with a magnificent sheen (from acetic acid) (Found : C, 63·4; H, 4·8%).

4′-Hydroxyflavylium perchlorate (1 g.) furnished 4′-*hydroxy*-4-(4′-*hydroxy*-4-*flavenylidenemethyl*)*flavylium perchlorate* (0·5 g.) in dark green needles, m. p. 280° (decomp.) (Found : C, 62·6; H, 4·4. $C_{31}H_{21}O_8Cl,2H_2O$ requires C, 62·8; H, 4·0%).

4′-Methoxyflavylium perchlorate (1 g.) gave 4′-*methoxy*-4-(4′-*methoxy*-4-*flavenylidenemethyl*)-*flavylium perchlorate* (0·5 g.) in deep green needles, m. p. 281° (decomp.) (Found : C, 67·3; H, 4·3. $C_{33}H_{25}O_8Cl$ requires C, 67·8; H, 4·3%).

4′-Hydroxy-8-methoxyflavylium perchlorate (1 g.) furnished 4′-*hydroxy*-4-(4′-*hydroxy*-8-*methoxy*-4-*flavenylidenemethyl*)-8-*methoxyflavylium perchlorate* (0·3 g.) in olive green needles, m. p. 330° (decomp.) (Found : C, 64·2; H, 4·2. $C_{33}H_{25}O_{10}Cl$ requires C, 64·3; H, 4·1%).

The free bases or the picrates from the foregoing products were not obtained crystalline.

3-Phenyl-, 3-methoxy-, 4-phenyl-, 5 : 7-dimethyl-, and 5 : 7-dimethoxy-flavylium perchlorate failed to condense with malonic acid and in most cases were recovered in 80—90% yield.

The analyses were performed by Mr. A. S. Inglis, M.Sc., and his associates of this Department.

UNIVERSITY OF LIVERPOOL. [*Received, November 11th*, 1956.]

[6] Wizinger, personal communication.

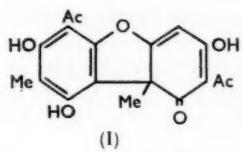
XUM

303. *Usnic Acid. Part XIII.* The Orientation and Synthesis of Usnolic Acid.*

By F. M. Dean, C. A. Evans, Thomas Francis, and Alexander Robertson.

In an extension of earlier work,[1] di-*O*-methylpyrousnic acid has been acylated to give 5-*O*-methylusnetic acid, the acetate of which furnished 7-acetyl-6-hydroxy-4-methoxy-3′-methoxycarbonyl-5 : 2′-dimethyl-3-methylene-4′-oxo*cyclo*pent-2′-ene-1′-*spiro*-2-coumaran identical with methyl *O*-methylusnolate, thus proving that usnolic acid has the same pattern of aromatic substitution as has usnic acid. Usnetic acid from the demethylation of 4-*O*-methylusnetic acid was converted by the standard method into methyl usnolate, the hydrolysis of which gave usnolic acid identical with the isomerisation product of usnic acid.

In Part IX [1] it was shown that the isomerisation of usnic acid (I) by sulphuric acid involved a ring contraction which, on the assumption that the aromatic rings of the isomers were identical, led to the development of structure (II; R = H) for usnolic acid. However, the heterocyclic system in structure (II) is a modified allyl ether grouping, and as such might well have been cleaved by the reagent with subsequent re-cyclisation involving the alternative hydroxyl group, whereupon structure (III) would be correct for usnolic acid. The synthesis of the *spiro*coumaran (II; R = Me), identical with methyl *O*-methyl-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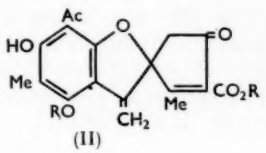
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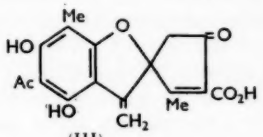
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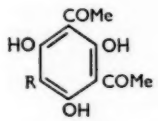
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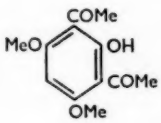
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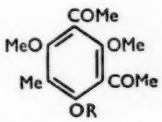
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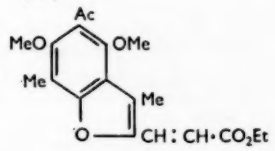

(VII)

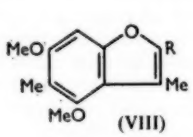
usnolate formed from usnolic acid, has now provided proof that the structure (II; R = H) suggested originally for usnolic acid is correct; in parallel work usnolic acid itself has been synthesised.

In preliminary investigation, 2 : 4-diacetyl-6-methylphloroglucinol (IV; R = Me) appeared to offer advantages as a starting material for the synthesis of compounds of types (II) and (III) because it already contained all the necessary aromatic substituents and because its lower homologue (IV; R = H) could be selectively methylated [2] to the phenol (V) containing an *o*-hydroxycarbonyl grouping necessary for elaboration of the *spiro*-coumaran system by well-established methods.[1] Unfortunately, phenol (IV; R = Me) gave only mixtures of mono- and tri-methyl ethers when selective alkylation was attempted. Further, the dimethyl ether (VI; R = H), available indirectly from (IV; R = Me), failed to react with ethyl bromoacetate, except at relatively high temperatures where a very small quantity of the desired phenoxyacetic ester (VI; R = $CH_2 \cdot CO_2Et$) resulted. On the other hand, the dimethyl ether (VI; R = H) reacted readily with allyl bromide giving (VI; R = $CH_2 \cdot CH{:}CH_2$) which was a typical allyl ether in that hydrogenation

* Part XII, *J.*, 1956, 2322.

[1] Dean, Halewood, Mongkolsuk, Robertson, and Whalley, *J.*, 1953, 1250.
[2] Dean and Robertson, *J.*, 1953, 1241.

resulted in a mixture of the parent phenol (VI; R = H) and the propyl ether (VI; R = Pr) identical with material formed by direct propylation. Although ethyl γ-bromocrotonate behaved like allyl bromide rather than ethyl bromoacetate and gave the phenoxycrotonate (VI; R = CH_2·CH:CH·CO_2Et), this resinified both when hydrolysis of the ester grouping was attempted and when efforts were made to induce dehydration to the coumarone (VII) which might have been a useful intermediate.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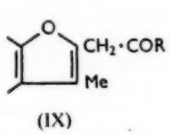
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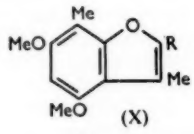
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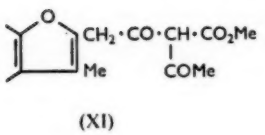
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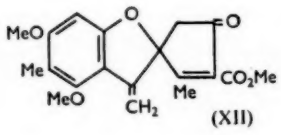
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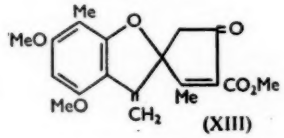
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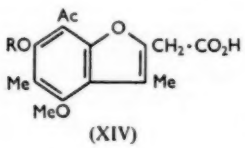
A relatively convenient preparation of 4 : 6-dimethoxy-3 : 5-dimethylcoumarilic acid (VIII; R = CO_2H) has been described.[3] Catalysed by copper carbonate, decarboxylation of this acid furnished the coumarone (VIII; R = H) from which the aldehyde (VIII; R = CHO) and thence the pyruvic acid (IX; R = CO_2H) were made by the method of Birch and Robertson.[4] When modified, the oxidation of this pyruvic acid to the acetic acid (di-*O*-methylpyrousnic acid) (IX; R = OH) gave satisfactory results, whereupon application of the same sequence of reactions to the coumarilic acid (X; R = CO_2H) gave the corresponding acetic acid (X; R = CH_2·CO_2H). The acids (IX; R = OH)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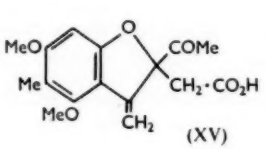
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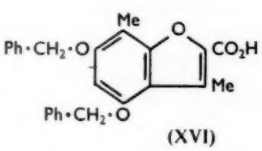
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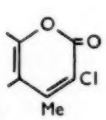
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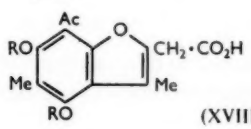

(XVIII)

and (X; R = CH_2·CO_2H) were transformed into the acid chlorides which, with the methoxymagnesio-derivative of methyl acetoacetate, gave diketo-esters type (XI) cyclised by sulphuric acid to the closely similar *spiro*coumarans (XII) and (XIII). It was not expected that insertion of an acetyl group into the free aromatic position of (XII) would be satisfactory because of the many reactive centres in the molecule, and, in practice, only gums resulted when this spiran was treated with acetic anhydride and boron fluoride. Attention was therefore directed to introduction of this acetyl group at an earlier stage in the synthesis.

Interaction of di-*O*-methylpyrousnic acid (IX; R = OH) and acetic anhydride in the presence of boron fluoride might have given, not only 4-*O*-methylusnetic acid (XIV; R = H) arising from the usual aromatic acylation accompanied by demethylation, but also an exomethylenecoumaran (XV) resulting from a reaction with acetylium formally parallel

[3] Dean, Evans, and Robertson, *J.*, 1954, 4565.
[4] Birch and Robertson, *J.*, 1938, 306.

to the acid-catalysed cyclisation of compounds of type (XI) to *spiro*coumarans. However, only the usnetic acid derivative (XIV; R = H) was isolated. The acid chloride from the corresponding acetate (XIV; R = Ac) was condensed with the methoxymagnesio-derivative of methyl acetoacetate and when treated with sulphuric acid the product was simultaneously cyclised and deacetylated, giving methyl *O*-methylusnolate (II; R = Me) identical with the ester obtained by alkylation of usnolic acid with diazomethane.[1]

Demethylation of methyl *O*-methylusnolate to usnolic acid was found to be impracticable; further, the use of the benzyl group for protection of the hydroxyl group was discounted because the dibenzyloxycoumarilic acid (XVI), though readily obtainable from the chlorocoumarin (XVII), could not be decarboxylated or converted into the homologous acetic acid by the Arndt–Eistert reaction. Fortunately, dealkylation of 4-*O*-methylusnetic acid with magnesium iodide gave a fair yield of usnetic acid (XVIII; R = H) identical with a sample from alkaline degradation of usnic acid, and, when subjected to the standard sequence of reactions, the corresponding diacetate (XVIII; R = Ac) furnished methyl usnolate identical with a sample prepared from usnolic acid.[1] At first, hydrolysis of methyl usnolate proved troublesome, but eventually conditions were found in which this ester was smoothly converted into usnolic acid (II; R = H) indistinguishable from an authentic specimen.

Experimental

2 : 4-*Diacetyl*-6-*methylphloroglucinol* (IV; R = Me).—Acetic acid (20 ml.), containing *C*-methylphloroglucinol triacetate (5·0 g.) was saturated with boron fluoride at −10° and 10 min. later the brown viscous mass was stirred into water (150 ml.), giving a yellow solid which was decomposed by dissolution in hot 50% alcohol. The resulting 2 : 4-diacetyl-6-methylphloroglucinol separated from the cooled solution, forming needles (4·0 g.), m. p. 170°, from dilute alcohol (Found: C, 58·8; H, 5·6. Calc. for $C_{11}H_{12}O_5$: C, 58·9; H, 5·4%).

Attempted dimethylation of this phenol (1·0 g.) in boiling acetone (50 ml.) with methyl sulphate (1·2 g., 2·2 mols.) and potassium carbonate (2·0 g.) during 4 hr. followed by removal of insoluble matter and solvent gave an orange gum partly soluble in 2N-aqueous sodium hydroxide. Crystallised from light petroleum (b. p. 60—80°), the insoluble fraction furnished 2 : 4-diacetyl-6-methylphloroglucinol trimethyl ether in prisms (0·4 g.), m. p. and mixed m. p. 66—67°. Regained by acidification of the alkaline solution, the soluble fraction crystallised from dilute alcohol, giving 2 : 4-diacetyl-6-methylphloroglucinol 1-methyl ether in needles (0·2 g.), m. p. and mixed m. p. 97°. The use of methyl iodide as the alkylating agent gave a similar result.

2 : 4-*Diacetyl*-6-*methylphloroglucinol* 1 : 3-*Dimethyl Ether* (VI; R = H).—Warmed on the steam-bath with N-aqueous sodium hydroxide (20 ml.), 2 : 4-diacetyl-6-methylphloroglucinol 5-acetate 1 : 3-dimethyl ether[2] (1·0 g.; m. p. 80°) dissolved in about 25 min. Liberated by hydrochloric acid and isolated with ether, the resulting 2 : 4-*diacetyl*-6-*methylphloroglucinol* 1 : 3-*dimethyl ether* separated from dilute alcohol in fine, pale yellow needles (0·6 g.), m. p. 64°, having a dark red ferric reaction in alcohol [Found: C, 61·6; H, 6·4; OMe, 24·5. $C_{11}H_{10}O_3(OMe)_2$ requires C, 61·9; H, 6·4; OMe, 24·6%]. The acetate used in this preparation formed platelets, m. p. 80°, but sometimes a second form was encountered which existed as cubes, m. p. 92° [Found: C, 61·2; H, 6·2; OMe, 20·9. Calc. for $C_{13}H_{12}O_4(OMe)_2$: C, 61·2; H, 6·2; OMe, 21·1%]. Acetylation of the phenol (VI) regenerated the acetate which could again be obtained in either form, but definite conditions for their interconversion could not be established.

Ethyl 2 : 4-*Diacetyl*-3 : 5-*dimethoxy*-6-*methylphenoxyacetate* (VI; R = $CH_2{\cdot}CO_2Et$).—The interaction of 2 : 4-diacetyl-6-methylphloroglucinol 1 : 3-dimethyl ether (1·0 g.) and ethyl bromoacetate (0·8 g.) in boiling diethyl ketone (25 ml.), containing potassium carbonate (1·0 g.), for 2 hr. gave a brown gummy product which was freed from phenolic material by means of 2N-aqueous sodium hydroxide and purified from benzene by use of an aluminium oxide column. Evaporation of the fawn eluate left a solid which furnished the *phenoxyacetate* in needles (50 mg.), m. p. 139—140°, after several recrystallisations fom light petroleum (b. p. 40—60°) [Found: C, 60·5; H, 6·2; alkoxyl (as OMe) 27·8. $C_{13}H_{11}O_4(OMe)_2{\cdot}OEt$ requires C, 60·3; H, 6·5; alkoxyl (as OMe) 27·5%]. When diethyl ketone was replaced by acetone, ethyl methyl ketone, or benzene, there was no reaction.

2 : 4-*Diacetyl*-6-*methylphloroglucinol* 5-*Allyl* 1 : 3-*Dimethyl Ether* (VI; R = CH_2·CH:CH_2).—Formed by the interaction of 2 : 4-diacetyl-6-methylphloroglucinol 1 : 3-dimethyl ether (1·0 g.), allyl bromide (1·0 g.), and potassium carbonate (2 g.) in boiling acetone (15 ml.) during 8 hr., the oil gave on distillation the *allyl ether* (VI; R = CH_2·CH:CH_2) (0·8 g.), b. p. 170° (bath)/0·05 mm., with a negative ferric reaction (Found: C, 65·2; H, 6·7. $C_{16}H_{20}O_5$ requires C, 65·7; H, 6·9%).

A solution of this allyl ether (1·0 g.) in methanol (150 ml.) containing 1% palladium–charcoal (1 g.) was shaken in hydrogen at ordinary pressure until absorption ceased. The oil left when the catalyst and solvent were removed was partly soluble in 2N-aqueous sodium hydroxide; the alkaline washings of this contained 2 : 4-diacetyl-6-methylphloroglucinol 1 : 3-dimethyl ether (0·4 g.), m. p. and mixed m. p. 64°, and the non-phenolic material supplied **2 : 4-*diacetyl*-6-*methylphloroglucinol* 1 : 3-*dimethyl* 5-n-*propyl ether*** (0·5 g.), b. p. 120° (bath)/0·05 mm. (Found: C, 65·6; H, 7·6. $C_{16}H_{22}O_5$ requires C, 65·3; H, 7·5%). Comparison of infrared spectra identified this propyl ether with the product obtained by the action of propyl iodide on 2 : 4-diacetyl-6-methylphloroglucinol 1 : 3-dimethyl ether in the potassium carbonate–acetone method.

Ethyl* γ-(2 : 4-*Diacetyl*-3 : 5-*dimethoxy*-6-*methylphenoxy*)*crotonate (VI; R = CH_2·CH:CH·CO_2Et).—In 6 hr., the purple colour of a mixture of 2 : 4-diacetyl-6-methylphloroglucinol 1 : 3-dimethyl ether (1·0 g.), ethyl γ-bromocrotonate (1·5 g.) and potassium carbonate (2·0 g.) in boiling acetone had faded to yellow. The alkali-insoluble product crystallised from light petroleum (b. p. 40—60°), giving the *phenoxycrotonate* in needles (1·3 g.), m. p. 94°, having a negative ferric reaction (Found: C, 62·9; H, 6·6. $C_{19}H_{24}O_7$ requires C, 62·6; H, 6·6%). In hot alcoholic sodium ethoxide or dilute sodium hydroxide this ester rapidly resinified.

4 : 6-*Dibenzyloxy*-3 : 7-*dimethylcoumarilic Acid* (XVI).—The reaction between 3-chloro-5 : 7-dihydroxy-4 : 8-dimethylcoumarin [3] (10 g.) and benzyl bromide (15·5 g.) in boiling acetone (200 ml.), containing potassium carbonate (20 g.), gave after 4 hr. the **5 : 7-*dibenzyloxy*-3-*chloro*-4 : 8-*dimethylcoumarin*** (XVII) which separated from benzene in needles (15 g.), m. p. 223° (Found: C, 71·5; H, 4·9. $C_{25}H_{21}O_4Cl$ requires C, 71·3; H, 5·0%).

This dibenzyloxycoumarin (2 g.) was added to potassium hydroxide (0·6 g.) in boiling "Carbitol" (50 ml.) and, 10 min. later, the mixture was diluted with an equal volume of water and acidified with hydrochloric acid, liberating crude **4 : 6-*dibenzyloxy*-3 : 7-*dimethylcoumarilic acid***, which, purified from dilute methanol (charcoal), formed biprisms (1·5 g.), m. p. 210° (decomp.) (Found: C, 74·9; H, 5·5. $C_{25}H_{22}O_5$ requires C, 74·6; H, 5·5%). A solution of this acid in warm sulphuric acid had a violet tinge. The *methyl ester* (diazomethane) separated from methanol in white needles, m. p. 116—118° (Found: C, 75·0; H, 5·8. $C_{26}H_{24}O_5$ requires C, 75·0; H, 5·8%).

This coumarilic acid was stable in boiling "Carbitol," glycerol, or quinoline with or without the addition of copper compounds. The acid chloride formed by the action of phosphorus pentachloride on the acid or of thionyl chloride on the sodium salt was a greenish solid which with ethereal diazomethane at −2° during 24 hr. gave a yellow, crude diazo-ketone. No identifiable products were obtained when this diazo-ketone was treated with silver oxide or silver benzoate in methanol, or heated in benzyl alcohol and dimethylaniline.

4 : 6-*Dimethoxy*-3 : 5-*dimethylcoumarone* (VIII; R = H).—Carbon dioxide was rapidly evolved for 10 min. from a mixture of 4 : 6-dimethoxy-3 : 5-dimethylcoumarilic acid (5 g.) and copper carbonate (0·5 g.) at 220°; distillation of the product gave 4 : 6-dimethoxy-3 : 5-dimethylcoumarone, b. p. 125° (bath)/0·05 mm., as a yellow oil (3·0 g.) which gave a purple colour in warm sulphuric acid [Found: C, 69·6; H, 7·0; OMe, 29·6. Calc. for $C_{10}H_8O(OMe)_2$: C, 69·9; H, 6·8; OMe, 30·1%].

4 : 6-*Dimethoxy*-3 : 5-*dimethylcoumaron*-2-*ylacetic Acid* (*Di*-O-*methylpyrousnic Acid*) (IX; R = OH).[4]—4 : 6-Dimethoxy-3 : 5-dimethylcoumaron-2-ylpyruvic acid (1·5 g.), dissolved in 2N-aqueous sodium hydroxide (15 ml.) at −5°, was oxidised with hydrogen peroxide (100-vol.; 1 ml.). Five min. later, slow acidification of the mixture precipitated the crude product which was isolated with ether and purified from benzene on aluminium oxide. The eluate furnished di-*O*-methylpyrousnic acid as prisms (0·9 g.), m. p. 127°, from benzene and then from dilute methanol [Found: C, 63·4; H, 6·2; OMe, 23·6. Calc. for $C_{12}H_{10}O_3(OMe)_2$: C, 63·6; H, 6·1; OMe, 23·5%].

4-O-*Methylusnetic Acid* (XIV; R = H).—Acetic acid (2 ml.) containing di-*O*-methylpyrousnic acid (0·8 g.) and acetic anhydride (0·6 g.) was saturated with boron fluoride without

cooling. Next day, the mixture was diluted with water, the dark green acidic oil was isolated with ether, and the ethereal solution extracted with aqueous sodium hydrogen carbonate. Acidification of the extract supplied 4-*O*-methylusnetic acid, crystallising from benzene (charcoal) in needles (0·8 g.), m. p. 166°, giving a green ferric reaction in alcohol (Found: C, 61·9; H, 5·6; OMe, 10·5. $C_{14}H_{13}O_8$·OMe requires C, 61·6; H, 5·5; OMe, 10·6%). Obtained from 4-*O*-methylusnetic acid (500 mg.) with acetic anhydride containing a trace of sulphuric acid, the *acetate* separated from benzene in needles (450 mg.), m. p. 134° (Found: C, 61·6; H, 5·8. $C_{17}H_{18}O_7$ requires C, 61·1; H, 5·4%).

Usnetic Acid (XVIII; R = H).—An intimate mixture of 4-*O*-methylusnetic acid (0·4 g.) and magnesium iodide (1·5 g.) was kept in nitrogen for 1 hr. at 190°. The solid remaining when the product was boiled with 2N-sulphuric acid (75 ml. × 2) was dissolved in ether and extracted into aqueous sodium hydrogen carbonate. After clarification of the extract with charcoal, acidification with hydrochloric acid furnished usnetic acid which crystallised in needles (0·1 g.), m. p. and mixed m. p. 198—199°; the identity with a natural specimen was confirmed by comparison of the infrared spectra.

Acetylation of this acid (0·5 g.) was effected by acetic anhydride and a trace of sulphuric acid in 2 hr. Purified by precipitation with light petroleum (b. p. 60—80°) from a solution in ethyl acetate, the *diacetate* then separated from aqueous methanol in needles (0·25 g.), m. p. 173°, having a negative ferric reaction (Found: C, 59·9; H, 5·1. $C_{18}H_{18}O_8$ requires C, 59·7; H, 5·0%).

2-Formyl-4 : 6-dimethoxy-3 : 7-dimethylcoumarone (X; R = CHO).—On decarboxylation by the method used for the 3 : 5-dimethyl isomeride, 4 : 6-dimethoxy-3 : 7-dimethylcoumarilic acid (5 g.) gave 4 : 6-dimethoxy-3 : 7-dimethylcoumarone (3·0 g.), b. p. 140° (bath)/0·05 mm., solidifying to prisms, m. p. 95—96° [Found: C, 69·9; H, 6·8; OMe, 30·2. Calc. for $C_{10}H_8O(OMe)_2$: C, 69·9; H, 6·8; OMe, 30·1%].

A solution of this coumarone (3·0 g.) in ether (75 ml.), containing zinc chloride (0·2 g.) and hydrogen cyanide (3 ml.), was saturated at 0° with hydrogen chloride and 3 days later the resulting green aldimine hydrochloride was collected, washed with ether, and hydrolysed with boiling water for 10 min. The *2-formylcoumarone* (X; R = CHO) separated in small yellow rhombs (3·0 g.) and had the same form, m. p. 158°, when purified from dilute methanol and then benzene [Found: C, 66·6; H, 6·2; OMe, 26·9. $C_{11}H_8O_3(OMe)_2$ requires C, 66·7; H, 6·0; OMe, 26·5%]. On being warmed, the yellow solution of this aldehyde in sulphuric acid became purple. The *rhodanine derivative* crystallised from acetone in dark red needles, m. p. 298° [Found: C, 55·0; H, 4·6; N, 3·8; OMe, 17·6. $C_{14}H_9O_2NS_2(OMe)_2$ requires C, 55·0; H, 4·3; OMe, 17·7%], and gave intractable gums when hydrolysed.

4 : 6-Dimethoxy-3 : 7-dimethylcoumarone-2-acetic Acid (X; R = CH_2·CO_2H).—A mixture of 2-formyl-4 : 6-dimethoxy-3 : 7-dimethylcoumarone (3·0 g.), hippuric acid (5·0 g.), sodium acetate (4·0 g.), and acetic anhydride (20 ml.) was kept on a steam-bath for 1·5 hr. and then macerated with 50% alcohol (100 ml.). Next day the solid was washed with water (300 ml.) and crystallised from acetone, giving the *azlactone* in orange needles, m. p. 238° [Found: C, 69·6; H, 4·8; N, 3·6; OMe, 16·6. $C_{20}H_{13}O_3N(OMe)_2$ requires C, 70·0; H, 5·1; N, 3·7; OMe, 16·4%].

After 10 hours, ammonia was no longer evolved from a boiling mixture of this azlactone (4 g.) and potassium hydroxide (8 g.) in 50% alcohol (40 ml.) which was then cooled, diluted with an equal volume of water, and saturated with sulphur dioxide. Three hours later, the tarry precipitate was removed and the clear solution was warmed with hydrochloric acid (15 ml.) on a steam-bath for 20 min. Thus precipitated, the crude pyruvic acid was purified from benzene, forming needles (1·7 g.), m. p. 196°, which did not give consistent analytical results. A solution of the crude acid (1·7 g.) in 2N-aqueous sodium hydroxide (15 ml.) at −5° was treated with hydrogen peroxide (100-vol.; 1 ml.) as for the 3 : 5-dimethyl isomeride and on purification from dilute methanol (charcoal) and then benzene the product furnished *4 : 6-dimethoxy-3 : 7-dimethylcoumaron-2-ylacetic acid* in needles (1·0 g.), m. p. 158—159°, giving a purple solution in warm sulphuric acid [Found: C, 64·0; H, 6·4; OMe, 23·7. $C_{12}H_{10}O_3(OMe)_2$ requires C, 63·6; H, 6·1; OMe, 23·5%].

4 : 6-Dimethoxy-3′-methoxycarbonyl-5 : 2′-dimethyl-3-methylene-4′-oxocyclopent-2′-ene-1′-spiro-2-coumaran (XII).—A mixture of magnesium powder (0·12 g.), absolute methanol (0·18 g.), methyl acetoacetate (0·6 g.), and a drop of carbon tetrachloride was heated gently under reflux until no further change occurred, diluted with anhydrous ether (10 ml.), boiled for a further 2 hr.,

and treated with an ethereal solution (40 ml.) of 4 : 6-dimethoxy-3 : 5-dimethylcoumaron-2-ylacetyl chloride which was prepared from the coresponding acid (1·0 g.) and phosphorus pentachloride (1·0 g.) in chloroform by the standard method. Next day, the mixture was boiled for 1 hr. and then treated with a slight excess of 2N-acetic acid, whereupon evaporation of the ethereal layer left the crude diketo-ester type (XI) as a reddish oil. On treatment with sulphuric acid (2·5 ml.) at 0° for 2 days followed by the addition of ice, this oil gave a gum which was dissolved in ether, washed with aqueous sodium hydrogen carbonate, and recovered. Triturated with methanol, the gum crystallised and was purified by adsorption of the impurities on aluminium oxide from a benzene solution. Crystallised from dilute methanol, the solid then furnished the 5 : 2′-*dimethyl*-spiro-2-*coumaran* in needles (0·6 g.), m. p. 141° $\lambda_{max.}$ 235, 267, 323 mμ (10^{-3} ε 28·2, 14·8, 11·3), which had blue Ehrlich and Légal reactions [Found : C, 66·0; H, 5·9; OMe, 27·0. $C_{16}H_{11}O_3(OMe)_3$ requires C, 66·3; H, 5·8; OMe, 27·0%].

4 : 6-*Dimethoxy*-3′-*methoxycarbonyl*-7 : 2′-*dimethyl*-3-*methylene*-4′-*oxo*cyclo*pent*-2′-*ene*-1′-spiro-2-*coumaran* (XIII) was prepared from 4 : 6-dimethoxy-3 : 7-dimethylcoumaron-2-ylacetic acid (1·0 g.) by the method given above for the isomeride (XII) and on crystallisation from methanol, formed yellow cubes (0·8 g.), m. p. 143°, $\lambda_{max.}$ 223, 233, 287 mμ (10^{-3} ε 27·5, 27·5, 19·1), having a deep blue reaction in the Ehrlich and Légal tests [Found : C, 66·0; H, 5·9; OMe, 27·0%].

Methyl 4-O-*Methylusnolate* (II; R = Me).—4-*O*-Methylusnetic acid 6-acetate (1·0 g.), dissolved in chloroform (15 ml.), was converted into the acid chloride by phosphorus pentachloride (0·7 g.) at room temperature for 15 min. and then under reflux for 30 min. After the removal of the solvent and phosphorus oxychloride, a solution of the red product in ether was added to the methoxymagnesio-derivative of methyl acetoacetate (from 0·35 ml. of ester), and the mixture refluxed for 1 hr. before the addition of 2N-acetic acid (10 ml.). Unchanged 4-*O*-methylusnetic acid acetate (0·2 g.) was removed from the ethereal layer by aqueous sodium hydrogen carbonate. Evaporation of the dried (Na_2SO_4) ether solution then left a viscous orange oil which was treated with sulphuric acid (2·5 ml.) at −2° for 2 days. An ethereal solution of the gummy solid, which was precipitated by the addition of ice, was washed with sodium hydrogen carbonate solution to remove acid and then with water, dried (Na_2SO_4), and evaporated. In contact with methanol, the residue crystallised and could then be recrystallised from that solvent, giving methyl *O*-methylusnolate in yellow prisms (0·25 g.), m. p. 131°, undepressed on admixture with a natural specimen, m. p. 134° (Found : C, 64·5; H, 5·7. Calc. for $C_{20}H_{20}O_7$: C, 64·5; H, 5·4%) Confirmation of this identity was obtained from a comparison of infrared spectra of the two specimens.

Usnolic Acid (II; R = H).—An ethereal solution of the acid chloride from usnetic acid diacetate (0·5 g.) and phosphorus pentachloride (0·32 g.) was added to the methoxymagnesio-derivative of methyl acetoacetate (from 0·16 ml. of ester), and the mixture heated under reflux for 1 hr. The resulting diketo-ester type (XI) was kept with sulphuric acid (1·25 ml.) at −2° for 2 days, and an ethereal solution of the sticky product obtained by the addition of ice was washed with aqueous sodium hydrogen carbonate and evaporated. On being kept, the residue crystallised and was then chromatographed on a silica column (10 × 1 cm.) from 2 : 3 chloroform–benzene. The product, readily eluted by the same solvent, was crystallised from methanol and then from benzene, giving methyl usnolate in yellow needles (100 mg.), m. p. and mixed m. p. 202° (Found : C, 63·6; H, 5·2; OMe, 9·0. Calc. for $C_{18}H_{15}O_6{\cdot}OMe$: C, 63·7; H, 5·1; OMe, 8·7%). This ester and an authentic specimen gave identical infrared spectra.

Of the various techniques of hydrolysis and demethylation examined, only the following was satisfactory. Methyl usnolate (0·05 g.) was kept in sulphuric acid dihydrate (2·5 ml.) at 60° for 15 min. The cooled and diluted solution was shaken with ether from which the product was extracted into aqueous sodium hydrogen carbonate. On acidification, the extract supplied usnolic acid, crystallising from aqueous methanol in yellow plates (0·03 g.), m. p. and mixed m. p. 230° (Found : C, 63·1; H, 4·7. Calc. for $C_{18}H_{16}O_7$: C, 62·8; H, 4·7%). This acid and an authentic specimen gave identical infrared spectra.

The analyses were performed by Mr. A. S. Inglis, M.Sc., and his associates in this Department.

UNIVERSITY OF LIVERPOOL. [*Received, November 5th,* 1956.]

XUM

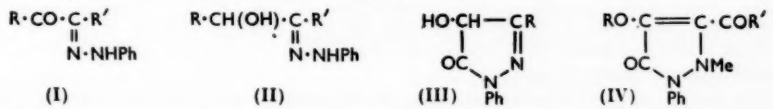
304. *The Reduction of Some α-Phenylhydrazono-ketones with Alkali Borohydrides.*

By R. E. Bowman and C. S. Franklin.

Several α-phenylhydrazono-ketones (I) have been reduced by alkali borohydrides to the corresponding alcohols (II) although in a few cases these proved too unstable for isolation. Some reactions of the alcohols have been examined, including hydrogenolysis as exemplified by the reduction of ethyl β-hydroxy-α-phenylhydrazonobutyrate (II; R = Me, R′ = CO_2Et) to an equimolar mixture of racemic and *allo*-threonine.

There appears to be no report of the reduction of phenylhydrazono-ketones of type (I) by alkali borohydrides and indeed, except for the sugar osazones, α-phenylhydrazono-alcohols (II) have received little study. This investigation had as object to obtain some members of this group and to develop a new route to α-amino-alcohols by their hydrogenolysis.

We began with two simple members, pyruvaldehyde and phenylglyoxylaldehyde monophenylhydrazones (I; R = Me and Ph respectively, R′ = H): with potassium or sodium borohydride in aqueous ethanol, at room temperature or slightly above, excellent yields of the alcohols (II; R = Me and Ph, R′ = H) were obtained. Analogous reductions took place with the monophenylhydrazones of ethyl αβ-dioxo-butyrate (I; R = Me, R′ = CO_2Et) and -succinate (R = R′ = CO_2Et) but in the latter case cyclisation of the product yielded the pyrazolone ester (III; R = CO_2Et).

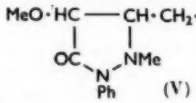


Similar reductive cyclisations occurred with other compounds of type (I) when R = CO_2Et; thus the esters (I; R = CO_2Et, R′ = CN or Ac) furnished the 4-hydroxypyrazol-5-ones (III; R = CN or CHMe·OH respectively), in the latter case further reduction of the 3-substituent yielding the corresponding secondary alcohol. The ester (III; R = CO_2Et) with methyl iodide in methanol at 110° furnished the 2-methyl derivative (IV; R = H, R′ = OEt) and we prepared a considerable number of such derivatives for biological evaluation. Although the anilide (IV; R = H, R′ = NHPh) could be prepared by interaction of the ester with anilinomagnesium iodide, the amide and hydrazide could not be obtained directly. However, the 4-hydroxyl group in these substances is phenolic (pK_a' 6·4) and the 4-methyl and 4-benzyl ether were readily obtained. These ethers, in contrast to the corresponding alcohols, reacted normally with ammonia and hydrazine, to give the corresponding amide and hydrazide; in the *O*-benzyl series, the benzyl group was removed by catalytic hydrogenolysis, yielding the hydroxy-amide and -hydrazide (R = H, R′ = NH_2, and $NH·NH_2$ respectively).

Esters (IV; R′ = OEt, R = H, Me, and CH_2Ph) were readily hydrolysed by alkali to the acids and, as with simple pyrazol-5-one-3-carboxylic acids, these lost carbon dioxide at 180° to give the pyrazol-5-ones. We also examined the further reduction of the ester (IV; R = Me, R′ = OEt) where the 4-hydroxyl grouping is protected by methylation; with lithium borohydride good yields of the corresponding 3-hydroxymethyl-4-methoxy-compound were obtained, but with lithium aluminium hydride the sole product was the saturated pyrazolidone (V). The latter reduction contrasts with that of antipyrine itself which under apparently identical conditions gives the pyrazoline (VI) and a smaller quantity of dihydroantipyrine (VII).

Among further reductions, the monophenylhydrazone of αβ-dioxo-β-phenylpropionitrile (I; R = Ph, R′ = CN) appeared to react normally with potassium borohydride

but the only crystalline product isolated (in low yield) was the unsaturated nitrile (VIII), which presumably arose by elimination of water from the expected reduction product reacting in its tautomeric phenylazo- (IX) rather than in the alternative phenylhydrazone structure (II; R = Ph, R′ = CN); as would be expected, the unsaturated nitrile, unlike the other compounds described so far, was highly coloured. Reduction of the analogous



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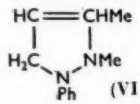

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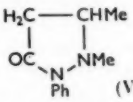
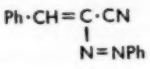


(VII)

nitro-compound (I; R = Ph, R′ = NO_2) was expected to take a similar course in view of the ready elimination of water from β-hydroxy-β-phenyl-α-nitroalkanes,[1] but a high yield of the nitro-alcohol (II; R = Ph, R′ = NO_2) was obtained. Catalytic reduction of the latter furnished a crystalline base which was shown by analysis and comparison with an authentic specimen obtained by interaction of ethyl mandelimidate[2] and phenylhydrazine to be the amidine (X).

Reduction of 2-oxo-2-phenyl-1-phenylhydrazonoethanesulphonic acid (I; R = Ph, R′ = SO_3H) was expected to be normal in view of the reported stability of 2-hydroxyalkane-1-sulphonic acids of which 2-hydroxy-2-phenylethanesulphonic acid is the nearest analogy.



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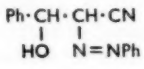
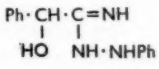


(IX)

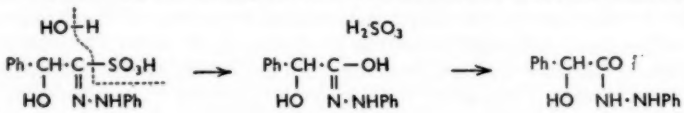


(X)

However, on acidification of the reduction mixture sulphur dioxide was evolved and chloroform extracted mandelic phenylhydrazide (XII), presumably formed from (XI) by hydrolysis and rearrangement.

Reaction of a phenylhydrazono-ketone containing two carbonyl functions, *viz.*, 3-phenylhydrazonopentane-2 : 4-dione (I; R = Me, R′ = Ac), with potassium borohydride was confined to one carbonyl group, yielding the 1 : 3-hydroxy-ketone (II; R = Me, R′ = Ac), under all conditions tried.

The ultraviolet absorption spectra of most of these compounds (see Table) fall into two groups: those possessing two strong bands at *ca.* 240 and 360—390 mμ where R or R′ are



(XI) (XII)

strong electron-attracting groups, and those with only one band at *ca.* 280 mμ which is usually associated with aliphatic non-conjugated phenylhydrazones and where R or R′ has weak or negligible activating effects. This difference could be useful in the diagnosis of phenylhydrazones possessing vicinal carbonyl groups.

Finally we examined the hydrogenolysis of a phenylhydrazono-alcohol in the presence of Raney nickel. Ethyl β-hydroxy-α-phenylhydrazonobutyrate (II; R = Me, R′ = CO_2Et) at atmospheric pressure slowly gave an oil, hydrolysis of which furnished DL-threonine and DL-*allo*threonine which were shown microbiologically to be present in equimolar proportion. However, the overall yield was low and the method does not compare favourably with the standard method in which the phenylhydrazone group is reduced before the carbonyl substituent.[3,4]

[1] Rosenmund, *Ber.*, 1913, **46**, 1037.
[2] Mackenzie, *J.*, 1918, 1.
[3] Pfister, Robinson, Shabica, and Tishler, *J. Amer. Chem. Soc.*, 1948, **70**, 2297.
[4] Bolhofer, *ibid.*, 1953, **75**, 4469.

Absorption spectra of some phenylhydrazones, RR'C:N·NHPh.

R	R'	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε
Ac	Ac	243	13,230	360	24,900
,,	CO_2Et	240	11,830	351	19,300
,,	$CO{\cdot}CO_2Et$	248	13,400	376	26,700
$CO{\cdot}CO_2Et$	CO_2Et	243	12,380	363	20,820
$CO{\cdot}CO_2Et$	CN	244	8,100	354	21,850
Bz	NO_2	246	13,900	393	14,600
,,	CN	245	11,800	379	21,800
Ac	H	237	10,090	350	22,460
,,	CHMe·OH	236	11,100	341	21,350
Me	CO_2Et	223	10,070	324	21,140
CHMe·OH	CO_2Et	231	9,830	329	20,900
Bz	H	247	14,150	380	19,810
CHPh·OH	NO_2	238	15,400	400	13,400
CHMe·OH	H	—	—	277	18,200
$Ph{\cdot}CH_2$	H	—	—	281	18,470
CHPh·OH	H	—	—	280	19,020
,,	NH_2	—	—	267	12,000
Ph·CH:C(CN)·N:NPh		236	7,500	348	40,000

Experimental

Ultraviolet absorption spectra were determined for EtOH solution, the Unicam S.P. 500 Spectrophotometer being used. Light petroleum was the fraction of b. p. 60—80°.

Reduction of α-Phenylhydrazono-ketones.—Method A. A 1% solution of sodium or potassium borohydride (0·5 mol.) in aqueous ethanol (H_2O : EtOH, 3 : 1) was added dropwise with stirring to a solution of the phenylhydrazono-ketone (1 mol.) in ethanol and after 1—2 hr. at 20—40° the mixture was concentrated *in vacuo*. The phenylhydrazono-alcohol was isolated by extraction with ethyl acetate and crystallised from benzene–light petroleum, except where otherwise stated.

Method B. The procedure was the same but the reaction temperature was kept below 25° and the solution acidified with 2N-sulphuric acid at the end of the reduction; after removal of the inorganic salts by filtration, the product was isolated as before.

Method C. The reduction was carried out as for method *B* but in an atmosphere of nitrogen and with an equimolar quantity of potassium borohydride (10% solution in water). On concentration of the filtered solution the product solidified and was purified by crystallisation. The following were thus obtained (method indicated in parentheses):

Lactaldehyde phenylhydrazone [5] [from pyruvaldehyde phenylhydrazone [6] (*A*)], prisms (53%), m. p. 90·5—91·5° (Wöhl gives m. p. 93°) (Found: C, 66·4; H, 7·6; N, 16·7. Calc. for $C_9H_{12}ON_2$: C, 65·8; H, 7·4; N, 17·1%).

Mandelaldehyde phenylhydrazone [from phenylglyoxylaldehyde phenylhydrazone [7] (*A*)], needles, m. p. 103° (Found: C, 74·3; H, 6·2; N, 12·0. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2; N, 12·4%).

4-Oxo-3-phenylhydrazonopentan-2-ol [from 3-phenylhydrazonopentane-2 : 4-dione [8] (*A*)], yellow needles (40%), m. p. 138—138·5° (Found: C, 64·2; H, 6·7; N, 13·6. $C_{11}H_{14}O_2N_2$ requires C, 64·1; H, 6·8; N, 13·6%).

Ethyl β-hydroxy-α-phenylhydrazonobutyrate [from ethyl β-oxo-α-phenylhydrazonobutyrate [9] (*B*)], prisms (55%), m. p. 93—94° (Found: C, 61·1; H, 6·8; N, 11·5. $C_{12}H_{16}O_3N_2$ requires C, 61·0; H, 6·8; N, 11·9%).

β-Phenyl-α-phenylazoacrylonitrile [from β-oxo-β-phenyl-α-phenylhydrazonopropionitrile [10] (*B*)], orange needles (11%), m. p. 119—120° (Found: C, 77·1; H, 4·7; N, 18·1. $C_{15}H_{11}N_3$ requires C, 77·2; H, 4·8; N, 18·0%).

2-Nitro-1-phenyl-2-phenylhydrazonoethanol [from the corresponding nitro-ketone [11] (*B*)],

[5] Wöhl, *Ber.*, 1908, **41**, 3611.
[6] Japp and Klingemann, *J.*, 1888, **53**, 519.
[7] Muller and von Pechmann, *Ber.*, 1889, **22**, 2557.
[8] Bulow, *Ber.*, 1902, **35**, 2188.
[9] *Idem*, *Ber.*, 1912, **45**, 3736.
[10] Haller, *Compt. rend.*, 1889, **108**, 1116.
[11] Parkes, *J.*, 1934, 67.

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deep orange needles (67%) (from xylene), m. p. 121—122° (Found: C, 62·3; H, 5·0; N, 15·1. $C_{14}H_{12}O_3N_2$ requires C, 62·0; H, 4·8; N, 15·5%).

Mandelic acid phenylhydrazide [12] [from 2-oxo-2-phenyl-1-phenylhydrazonoethanesulphonic acid [13] (*B*)], needles (13%) (from alcohol), m. p. and mixed m. p. 181—183° (Found: C, 69·6; H, 5·7. Calc. for $C_{14}H_{14}O_2N_2$: C, 69·4; H, 5·8%).

3-*Ethoxycarbonyl*-4-*hydroxyl*-1-*phenylpyrazol*-5-*one* [from ethyl α-oxo-β-phenylhydrazonosuccinate [14] (*C*)], needles (77%) (from ethyl acetate), m. p. 163°, $\lambda_{max.}$ 239, 357 mμ (ε 10,660, 17,720) (Found: C, 57·7; H, 4·7; N, 11·3. $C_{12}H_{12}O_4N_2$ requires C, 58·1; H, 4·9; N, 11·3%). Acetylation with acetic anhydride at 50° gave prisms, from benzene–light petroleum, of the *acetate*, m. p. 74—75°, $\lambda_{max.}$ 253 mμ (ε 10,170), $\lambda_{infl.}$ 275 mμ (ε 5700) (Found: C, 57·9; H, 4·7; N, 9·4. $C_{14}H_{14}O_5N_2$ requires C, 57·9; H, 4·9; N, 9·7%).

3-*Ethoxycarbonyl*-4-*hydroxy*-1-p-*nitrophenylpyrazol*-5-*one* [from ethyl α-oxo-β-*p*-nitrophenylhydrazonosuccinate [15] (*C*)], pale yellow prisms (50%) (from ethanol), m. p. 198° (decomp.), $\lambda_{max.}$ 228, 373 mμ (ε 11,400, 28,020) (Found: C, 48·7; H, 3·8; N, 14·5. $C_{12}H_{11}O_6N_3$ requires C, 49·1; H, 3·8; N, 14·3%).

3-*Cyano*-4-*hydroxy*-1-*phenylpyrazol*-5-*one* [from ethyl β-cyano-α-oxo-β-phenylhydrazonopropionate [16] (*C*)], needles (57%) (from nitromethane), m. p. 167° (decomp.), $\lambda_{max.}$ 252, 344 mμ (ε 14,100, 6300) (Found: C, 59·3; H, 3·7; N, 20·8. $C_{10}H_7O_2N_3$ requires C, 59·7; H, 3·5; N, 20·9%).

4-*Hydroxy*-3-1′-*hydroxyethyl*-1-*phenylpyrazol*-5-*one* [from ethyl αγ-dioxo-β-phenylhydrazonovalerate [17] (*C*)], prisms (26%) (from ethanol), m. p. 161° (decomp.), $\lambda_{max.}$ 241, 397 mμ (ε 14,800, 9750), pK_a' 7·9 in 50% ethanol (Found: C, 59·8; H, 5·5. $C_{11}H_{12}O_3N_2$ requires C, 60·0; H, 5·5%).

3-*Ethoxycarbonyl*-4-*hydroxy*-2-*methyl*-1-*phenylpyrazol*-5-*one*.—3-Ethoxycarbonyl-4-hydroxy-1-phenylpyrazol-5-one (50 g.), methyl iodide (28·4 g.), and methanol (50 ml.) were heated together in an autoclave at 105° for 16 hr. and, after cooling, the solid was filtered off and air-dried. Crystallisation from 50% aqueous ethanol (700 ml.) afforded needles of the N-*methylpyrazolone* (37 g.), m. p. 164°, $\lambda_{max.}$ 284, 331 mμ (ε 11, 210, 8110), pK_a' 6·4 in 50% methanol (Found: C, 59·6; H, 5·7; N, 10·8; active H, 0·37. $C_{12}H_{14}O_4N_2$ requires C, 59·5; H, 5·4; N, 10·7; 1 active H, 0·38%). Treatment with acetic anhydride gave the *acetate* as needles (from benzene–light petroleum), m. p. 71—72°, $\lambda_{max.}$ 237, 252, 317 mμ (ε 7330, 7710, 6910) (Found: C, 59·1; H, 5·3; N, 9·5. $C_{15}H_{16}O_5N_2$ requires C, 59·2; H, 5·3; N, 9·2%), whilst interaction with the appropriate acid chloride in the presence of pyridine yielded the following esters: *benzoate*, needles (from benzene–light petroleum), m. p. 115—116° (Found: C, 65·6; H, 4·8; N, 7·7. $C_{20}H_{18}O_5N_2$ requires C, 65·6; H, 5·0; N, 7·7%); *diphenylacetate*, plates (from benzene–light petroleum), m. p. 120—121° (Found: C, 70·6; H, 5·2; N, 6·4. $C_{27}H_{24}O_5N_2$ requires C, 71·0; H, 5·3; N, 6·1%); p-*nitrobenzoate*, pale yellow prisms (from 50% aqueous ethanol), m. p. 151° (Found: C, 58·0; H, 4·2; N, 9·9. $C_{20}H_{17}O_7N_3$ requires C, 58·4; H, 4·2; N, 10·2%). Hydrogenation of the last ester with palladised strontium carbonate gave the p-*aminobenzoate*, pale yellow needles (from ethanol), m. p. 186° (Found: C, 60·5; H, 4·8; N, 10·8. $C_{20}H_{19}O_6N_3$ requires C, 60·5; H, 4·8; N, 10·6%).

3-*Carboxy*-4-*hydroxy*-2-*methyl*-1-*phenylpyrazol*-5-*one*.—The ester (IV; R = H, R′ = OEt) (2 g.) in warm ethanol (35 ml.) was treated overnight with 2N-sodium hydroxide (2 mol.); after concentration *in vacuo* the solution was acidified with 2N-hydrochloric acid and the resulting solid filtered off. Crystallisation from aqueous ethanol gave needles of the *acid* (1·8 g.), m. p. 134° (decomp.), $\lambda_{max.}$ 269, 298 mμ (ε 10,070, 6980), pK_a' 3·2 and 10·2 in 50% methanol (Found: C, 56·3; H, 4·9; N, 11·5. $C_{11}H_{10}O_4N_2$ requires C, 56·4; H, 4·3; N, 12·0%). The acid was heated to 200° (bath) until the evolution of carbon dioxide had stopped and, on cooling, the melt solidified. Crystallisation from toluene yielded 4-*hydroxy*-2-*methyl*-1-*phenylpyrazol*-5-*one* as needles, m. p. 191—192°, $\lambda_{max.}$ 242, 247, 283 mμ (ε 9950, 10,100, 9100), pK_a' 9·3 in 50% methanol (Found: C, 63·1; H, 5·4; N, 14·7. $C_{10}H_{10}O_2N_2$ requires C, 63·2; H, 5·3; N, 14·7%).

4-*Hydroxy*-2-*methyl*-1-*phenyl*-3-N-*phenylcarbamoylpyrazol*-5-*one*.—The ester (IV; R = H, R′ = OEt) (1 g.) in dioxan (10 ml.) was added to a suspension of anilinomagnesium iodide

[12] Reissert, *Ber.*, 1889, **22**, 2928.
[13] Parkes, *J.*, 1934, 1861.
[14] Rabischong, *Bull. Soc. chim. France*, 1904, **31**, 78.
[15] Chattaway, *J.*, 1933, 1389.
[16] Fleischauer, *J. prakt. Chem.*, 1893, **47**, 382.
[17] Beyer and Claisen, *Ber.*, 1888, **21**, 1697.

(2 mol.) in ether (30 ml.) (Hardy's method [18]), the *anilide* being obtained as needles (0·3 g.) (from aqueous ethanol), m. p. 231—232° (decomp.), $\lambda_{max.}$ 294, 340 mμ (ε 20,800, 11,300), pK_a' 5·5 in 50% dimethylacetamide (Found: C, 66·3; H, 4·7; N, 13·2. $C_{17}H_{15}O_3N_3$ requires C, 66·0; H, 4·9; N, 13·6%).

4-Benzyloxy-3-ethoxycarbonyl-2-methyl-1-phenylpyrazol-5-one.—Benzyl chloride (12·7 g.) and the ester (IV; R = H, R′ = OEt) (13 g.) in ethyl methyl ketone (1 l.) were refluxed with stirring in the presence of anhydrous potassium carbonate (27 g.) for 16 hr. The mixture was cooled and filtered, the filtrate evaporated to dryness, and the residue crystallised from light petroleum, to give needles of the *benzyl ether* (16·5 g.), m. p. 84—85°, $\lambda_{max.}$ 265, 319 mμ (ε 8800, 7880) (Found: C, 68·1; H, 5·7; N, 8·1. $C_{20}H_{20}O_4N_2$ requires C, 68·2; H, 5·7; N, 8·0%). Hydrolysis as previously yielded nacreous plates (from aqueous ethanol) of *4-benzyloxy-3-carboxy-2-methyl-1-phenylpyrazol-5-one*, m. p. 171° (decomp.), $\lambda_{max.}$ 260 mμ (ε 10,000), $\lambda_{infl.}$ 253, 293 mμ (ε 8450, 8410), pK_a' 3·4 in 50% methanol (Found: C, 66·7; H, 4·9. $C_{18}H_{16}O_4N_2$ requires C, 66·7; H, 5·0%). The acid was decarboxylated as before, to *4-benzoyloxy-2-methyl-1-phenylpyrazol-5-one* which separated from benzene–light petroleum as needles, m. p. 125—126°, $\lambda_{max.}$ 245, 282 mμ (ε 8750, 8750), $\lambda_{infl.}$ 268 mμ (ε 7430) (Found: C, 72·3; H, 5·6. $C_{17}H_{16}O_2N_2$ requires C, 72·8; H, 5·8%).

3-Carbamoyl-4-hydroxy-2-methyl-1-phenylpyrazol-5-one.—The ether (IV; R = Ph·CH_2, R′ = OEt) (0·5 g.) in methanol (15 ml.) at 0° was treated with dry ammonia for 5 hr. Removal of the solvent by distillation and crystallisation of the residue from aqueous ethanol furnished needles of *4-benzyloxy-3-carbamoyl-2-methyl-1-phenylpyrazol-5-one* (0·45 g.), m. p. 120·5—121·5° (Found: N, 13·0. $C_{18}H_{17}O_3N_3$ requires N, 13·0%). This compound (0·75 g.) in absolute ethanol (20 ml.) was hydrogenated in the presence of palladised strontium carbonate in the usual manner, to give the *hydroxy-amide* (0·2 g.), m. p. 246° (decomp.), $\lambda_{max.}$ 282, 330 mμ (ε 8880, 5890), pK_a' 6·0 in 50% methanol (Found: C, 56·7; H, 4·8; N, 17·6. $C_{11}H_{11}O_3N_3$ requires C, 56·7; H, 4·8; N, 18·0%), as needles from aqueous ethanol.

Hydrazide of 3-Carboxy-4-hydroxy-2-methyl-1-phenylpyrazol-5-one.—4-Benzyloxy-3-ethoxycarbonyl-2-methyl-1-phenylpyrazol-5-one (1 g.) in ethanol (10 ml.) was refluxed for 3 hr. with hydrazine hydrate (2 ml.; 90% w/w). On concentration to a small volume and addition of water (5 ml.) the crude *hydrazide* separated; it crystallised from water as needles (0·6 g.), m. p. 115° (Found: N, 16·4. $C_{18}H_{18}O_3N_4$ requires N, 16·6%). Hydrogenation as above gave, on crystallisation from aqueous alcohol, the *hydroxy-hydrazide* as plates (0·2 g.), m. p. 214° (decomp.), $\lambda_{max.}$ 289, 344 mμ (ε 12,450, 7850) (Found: C, 53·4; H, 4·8; N, 22·3. $C_{11}H_{12}O_3N_4$ requires C, 53·2; H, 4·9; N, 22·6%).

3-Ethoxycarbonyl-4-methoxy-2-methyl-1-phenylpyrazol-5-one.—The ester (IV; R = H, R′ = OEt) (13 g.) was added portionwise to a stirred solution at 10° of diazomethane (3 mol.) in ether (500 ml.) and after all the solid had dissolved acetic acid was added dropwise until no more effervescence occurred. The solution was washed with 2N-potassium carbonate, then water, and dried. Distillation to dryness and crystallisation of the residue from light petroleum yielded needles of the *methoxy-ester* (11·6 g.), m. p. 77°, $\lambda_{max.}$ 263, 318 mμ (ε 8090, 6590) (Found: C, 60·9; H, 6·1. $C_{14}H_{16}O_4N_2$ requires C, 60·9; H, 5·8%). Hydrolysis of the latter (6 g.) in the usual manner afforded *3-carboxy-4-methoxy-2-methyl-1-phenylpyrazol-5-one* as needles (from aqueous ethanol) (4·6 g.), m. p. 185° (decomp.), $\lambda_{max.}$ 259 mμ (ε 8800), $\lambda_{infl.}$ 295 mμ (ε 7120) (Found: C, 57·8; H, 5·1. $C_{12}H_{12}O_4N_2$ requires C, 58·1; H, 4·9%). Heating the acid at 185° gave *4-methoxy-2-methyl-1-phenylpyrazol-5-one*, prisms (from benzene–light petroleum), m. p. 118—120°, $\lambda_{max.}$ 245, 251, 281 mμ (ε 10,100, 9720, 9990) (Found: C, 64·7; H, 5·8. $C_{11}H_{12}O_2N_2$ requires C, 64·7; H, 5·9%), also obtained by the action of diazomethane on 4-hydroxy-2-methyl-1-phenylpyrazol-5-one.

3-Hydroxymethyl-4-methoxy-2-methyl-1-phenylpyrazol-5-one.—To a stirred suspension of lithium borohydride [19] (2 mol.) in tetrahydrofuran (25 ml.) was added dropwise the methoxy-ester (IV; R = Me, R′ = OEt) (7 g.) in ether (50 ml.) and after 30 min. the mixture was poured into water (100 ml.). Distillation to dryness *in vacuo* and crystallisation of the residue from water yielded needles of the *methoxy-alcohol* (4·1 g.), m. p. 155°, $\lambda_{max.}$ 247, 282 mμ (ε 10,800, 11,000) (Found: C, 61·5; H, 6·0. $C_{12}H_{14}O_3N_2$ requires C, 61·5; H, 6·0%).

3-Carbamoyl-4-methoxy-2-methyl-1-phenylpyrazol-5-one.—Dry ammonia was bubbled through a solution of the methoxy-ester (IV; R = Me, R = OEt) (10 g.) in methanol (30 ml.) at 0° for

[18] Hardy, *J.*, 1936, 398.
[19] Paul and Joseph, *Bull. Soc. chim. France*, 1953, 758.

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4 hr. Evaporation to dryness and crystallisation of the residue from water furnished prisms of the *amide* (6·7 g.), m. p. 125° (Found : C, 58·4; H, 5·3. $C_{12}H_{13}O_3N_3$ requires C, 58·3; H, 5·3%).

3-Cyano-4-methoxy-2-methyl-1-phenylpyrazol-5-one.—The foregoing amide (1 g.) and phosphoric oxide (1 g.) were mixed and distilled at atmospheric pressure over a free flame. The distillate, on crystallisation from light petroleum, afforded the *nitrile* as plates (0·5 g.), m. p. 89—90° (Found : C, 63·2; H, 5·0. $C_{12}H_{11}O_2N_3$ requires C, 62·9; H, 4·8%).

3-Ethoxycarbonyl-4-hydroxy-2-methyl-1-p-nitrophenylpyrazol-5-one.—3-Ethoxycarbonyl-4-hydroxy-1-*p*-nitrophenylpyrazol-5-one (2 g.), methyl iodide (15 g.), and methanol (5 ml.) were heated in a sealed tube at 110° for 15 hr. and, after cooling and filtration from unchanged material (0·2 g.), the filtrate was boiled with ethanol (15 ml.) and cooled. Filtration and crystallisation from ethanol gave yellow-brown cubes of the *N-methyl compound* (0·3 g.), m. p. 225—256° (decomp.), $\lambda_{max.}$ 314 mμ (ε 16,800) (Found : C, 50·6; H, 4·3. $C_{13}H_{13}O_6N_3$ requires C, 50·8; H, 4·3%). It formed an *acetate*, pale yellow prisms (from benzene–light petroleum), m. p. 117·5—118° (Found : C, 51·2; H, 4·2. $C_{15}H_{15}O_7N_3$ requires C, 51·6; H, 4·3%).

3-Hydroxymethyl-4-methoxy-2-methyl-1-phenylpyrazolid-5-one.—The methoxy-ester (IV; R = Me, R′ = OEt) (19 g.) in benzene (150 ml.) was added dropwise during 15 min. to a stirred and cooled suspension of lithium aluminium hydride (2·75 g.) in ether (100 ml.). The mixture was refluxed for 4 hr., then decomposed with water in the usual manner, and distillation yielded the *pyrazolidone* (8·8 g.), b. p. 149—151°/0·2 mm., n_D^{20} 1·5600 (Found : C, 61·4; H, 6·9. $C_{12}H_{16}O_3N_2$ requires C, 61·0; H, 6·8%).

2 : *3-Dimethyl-1-phenyl-Δ³-pyrazoline.*—Antipyrine (100 g.) in benzene (1·1 l.) was reduced with lithium aluminium hydride (20 g.) in ether (500 ml.) as in the previous example, and the crude product fractionally distilled, to give the *pyrazoline* (60 g.), b. p. 58°/0·2 mm., n_D^{20} 1·5708, pK_a' 3·72 in 66% ethanol (Found : C, 75·4; H, 8·2; N, 16·7. $C_{11}H_{14}N_2$ requires C, 75·8; H, 8·1; N, 16·1%). This formed a *sulphate* which, crystallised from ethanol–ether, had m. p. 160° (Found : C, 48·3; H, 5·9. $C_{11}H_{14}N_2,H_2SO_4$ requires C, 48·5; H, 5·9%). The pyrazoline on hydrogenation in the presence of palladised charcoal furnished 2 : 3-dimethyl-1-phenylpyrazolidine,[20] b. p. 68·5°/0·3 mm., n_D^{20} 1·5511, pK_a' 4·28 in 66% ethanol (Found : C, 74·7; H, 9·0; N, 16·1. Calc. for $C_{11}H_{16}N_2$: C, 75·0; H, 9·2; N, 15·9%). Dihydroantipyrine [21] was also isolated from the above reduction as a viscous liquid (14 g.), b. p. 112—114°/0·4 mm., n_D^{20} 1·5571, $\lambda_{max.}$ 253 mμ (ε 8130), pK_a' 9·05 in 66% ethanol (Found : C, 69·8; H, 7·6. Calc. for $C_{11}H_{14}ON_2$: C, 69·4; H, 7·4%).

N-Anilinomandelamidine.—Hydrogenation of 2-nitro-1-phenyl-2-phenylhydrazonoethanol (5·4 g.) in absolute ethanol (100 ml.) in the presence of palladised charcoal gave the *amidine* as prisms (from 50% aqueous ethanol) (3 g.), m. p. 132—134°, $\lambda_{max.}$ 267 mμ (ε 12,000), pK_a' 7·92 in 50% ethanol (Found : C, 70·0; H, 6·5; N, 17·3. $C_{14}H_{15}ON_3$ requires C, 69·7; H, 6·3; N, 17·4%). The base was heated in 2N-hydrochloric acid and cooled : the *hydrochloride* separated as needles, m. p. 210° (decomp.) (Found : C, 60·1; H, 6·0; N, 15·0. $C_{14}H_{15}ON_3,HCl$ requires C, 60·5; H, 5·8; N, 15·1%). This salt was also obtained when ethyl mandelimidate hydrochloride [2] (43 g.) and phenylhydrazine (21·6 g.) were refluxed together in absolute ethanol (200 ml.) for 30 min. After cooling and filtration from ammonium chloride (4 g.) the filtrate was diluted with ether to yield the salt (35 g.).

erythro- *and* threo-α-*Amino-β-hydroxybutyric Acid.*—Ethyl β-hydroxy-α-phenylhydrazonobutyrate (4·8 g.) in absolute ethanol (35 ml.) was hydrogenated at atmospheric pressure with Raney nickel W.6. Removal of the catalyst and evaporation of the filtrate to dryness afforded a residue to which was added water (25 ml.), and the suspension was refluxed for 4 hr. The resulting solution was then concentrated to dryness *in vacuo* and the residue crystallised from aqueous ethanol, to give the threonine mixture (15%), m. p. 222—224° (decomp.) (Found : C, 40·1; H, 7·5; N, 11·9. Calc. for $C_4H_9O_3N$: C, 40·3; H, 7·6; N, 11·8%). A microbiological assay (by Dr. O. D. Bird of the Nutrition Department, Parke, Davis & Company, Detroit, U.S.A.) showed the mixture to contain 23·6% of L-threonine.

Microanalyses were carried out by Mr. A. J. Durre whom the authors thank.

Research Department, Parke, Davis & Company, Ltd.,
Hounslow, Middlesex. [*Received, November 19th,* 1956.]

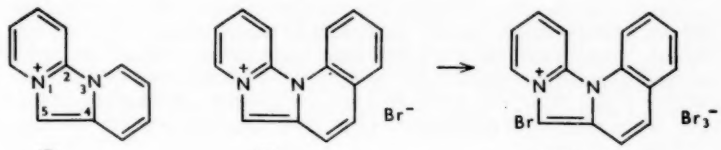
[20] Thoms, *Annalen*, 1923, **434**, 296.
[21] Knorr, *Ber.*, 1892, **25**, 759.

305. *Polynuclear Heterocyclic Systems. Part II.* Substitution Reactions of Condensed Glyoxalinium Salts.*

By B. R. Brown and D. White.

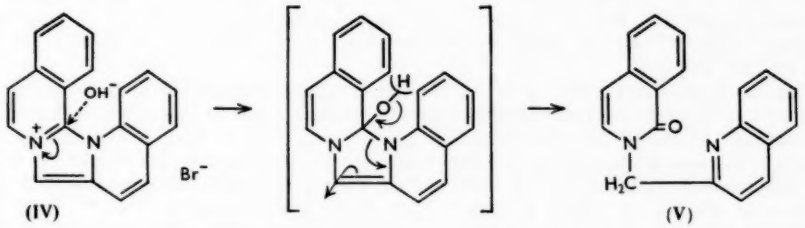
Bromination of pyridino(1′ : 2′-1 : 2)quinolino(1″ : 2″-3 : 4)glyoxalinium and diquinolino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)glyoxalinium salts has yielded compounds substituted in the 5-position. Sodium hydroxide disrupts the nucleus of diquinolinoglyoxalinium and quinolino(1′ : 2′-3 : 4)*iso*quinolino-(1″ : 2″-2 : 1)glyoxalinium salts with formation of *N*-2-quinolylmethylcarbostyril and -*iso*carbostyril respectively.

Consideration of the possible electronic shifts in the parent dipyridinoglyoxalinium cation (I) leads to the conclusion that substitution in the nucleus by cationoid reagents will occur at the 5-position, and that attack by anionoid reagents is favoured at the 2-position among others. The addition of further benzene nuclei, as in pyridinoquinolinoglyoxalinium (II), diquinolinoglyoxalinium, and quinolino*iso*quinolinoglyoxalinium salts (IV), does not alter the predictions.



(I) (II) (III)

Bromination of pyridinoquinolinoglyoxalinium bromide (II) in aqueous acetic acid affords 5-bromopyridinoquinolinoglyoxalinium perbromide (III) whose identity was proved by comparison with the compound synthesised as described in Part I.* Similarly, bromination of diquinolinoglyoxalinium perchlorate produces the 5-bromo-perbromide, which, for comparison, has been synthesised by one of the general methods previously described (Part I).



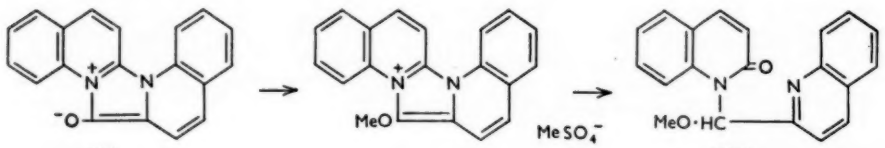
(IV) (V)

Aqueous sodium hydroxide, an anionoid reagent, destroys the nucleus, and the structure of the product confirms the glyoxalinium structures assigned to these compounds. Quinolino(1′ : 2′-3 : 4)*iso*quinolino(1″ : 2″-2 : 1)glyoxalinium bromide (IV) (synthesised by the standard method) yields *N*-2-quinolylmethyl*iso*carbostyril (V), whose structure has been confirmed by synthesis from *iso*carbostyril and ω-bromoquinaldine in the presence of methanolic potassium hydroxide.[1] Diquinolinoglyoxalinium bromide yields a compound which, from its ultraviolet and infrared spectra and by analogy with the reaction of quinolino*iso*quinolinoglyoxalinium bromide, must be *N*-2-quinolylmethylcarbostyril though attempts to synthesise this from ω-bromoquinaldine and carbostyril

* Part I, *J.*, 1956, 1158.

[1] Cf. Fernau, *Monatsh.*, 1893, **14**, 59.

failed (only starting materials or ωω-dibromoquinaldine, produced by disproportionation of the monobromo-compound,[2] has been isolated). Elucidation of the action of sodium hydroxide on glyoxalinium salts enables the formula (VII) to be assigned to the product obtained by Krollpfeiffer and Schneider[3] from Besthorn's Red (VI) by the action of methyl sulphate and alkali.



(VI) (VII)

Experimental

Pyridino(1′ : 2′-1 : 2)*quinolino*(1″ : 2″-3 : 4)*glyoxalinium Series.—Bromination of pyridinoquinolinoglyoxalinium bromide.* Pyridinoquinolinoglyoxalinium bromide (II) (0·90 g.) was dissolved in acetic acid (20 ml.) containing a few drops of water. Bromine (1·2 ml.) in acetic acid (10 ml.) was added gradually at 90° until bromine was in excess. The mixture was kept at 90° for 30 min., then cooled, and the yellow solid separated and washed with acetic acid and ether. Recrystallisation from acetic acid yielded yellow plates (0·75 g.) (Found : C, 33·8; H, 2·2. Calc. for $C_{15}H_{10}N_2Br_4$: C, 33·5; H, 1·85%). The infrared spectrum of the compound was identical with that of 5-bromopyridino(1′ : 2′-1 : 2)quinolino(1″ : 2″-3 : 4)glyoxalinium perbromide (Part I).

Treatment of this perbromide with pyridine yielded 5-bromopyridinoquinolinoglyoxalinium bromide which separated from methanol as pale yellow needles (Found : C, 47·8; H, 2·65. Calc. for $C_{15}H_{10}N_2Br_2$: C, 47·6; H, 2·65%). Infrared comparison proved the identity of the compound.

Diquinolino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)*glyoxalinium Series.—Bromination of diquinolinoglyoxalinium perchlorate.* Diquinolinoglyoxalinium perchlorate (0·90 g.) in aqueous acetic acid (80 ml.) was treated gradually with bromine in acetic acid at 90° until, after about 10 min., bromine was in slight excess and a permanent yellow precipitate had been produced. The mixture was cooled, and the solid collected, washed, and recrystallised from acetic acid to yield *5-bromodiquinolino*(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)*glyoxalinium perbromide* (0·90 g.) as pale yellow needles (Found : C, 38·8; H, 2·15; N, 4·6; Br, 54·3. $C_{19}H_{12}N_2Br_4$ requires C, 38·7; H, 2·05; N, 4·75; Br, 54·4%).

5-Bromodiquinolino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)*glyoxalinium bromide.* The above perbromide (0·90 g.) was treated with just insufficient pyridine (about 6 ml.) to dissolve it. The mixture was swirled vigorously and the colourless solution was filtered from the remaining solid. Overnight the solution became brown and yellow crystals were deposited. These were washed with ether and recrystallised twice from methanol–ether to yield yellow needles (0·20 g.) of the *bromide* (Found : C, 52·6; H, 3·05. $C_{19}H_{12}N_2Br_2,\frac{1}{2}CH_4O$ requires C, 52·7; H, 3·15%). The infrared spectrum of the compound contains a band at 3425 cm.$^{-1}$ characteristic of the solvent of crystallisation. The *perchlorate* prepared in water and crystallised from ethanol formed yellow-brown prisms (Found : C, 51·5; H, 2·75. $C_{19}H_{12}O_4N_2ClBr$ requires C, 51·0; H, 2·7%).

5-Bromodiquinolino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)*glyoxalinium perbromide.* 1-2′-Quinolylmethylquinolinium bromide[4] (0·20 g.), acetic acid (5·0 ml.), water (10 ml.), and sodium acetate (0·5 g.) were heated at 90° and treated dropwise with bromine in acetic acid until no further precipitation was observed. The yellow crystals were separated from the cold mixture, washed with acetic acid, and crystallised from acetic acid to yield yellow needles (0·11 g.) (Found : N, 4·55. Calc. for $C_{19}H_{12}N_2Br_4$: N, 4·75%). Infrared comparison showed the compound to be identical

[2] Brown, Grice, Hammick, and Thewlis, *J.*, 1951, 1149.
[3] Krollpfeiffer and Schneider, *Annalen*, 1937, **530**, 34.
[4] Hammick, Lammiman, Morgan, and Roe, *J.*, 1955, 2440.

with that prepared by the bromination of diquinolinoglyoxalinium perchlorate as described above.

Action of sodium hydroxide on diquinolinoglyoxalinium bromide. Diquinolinoglyoxalinium bromide (0·20 g.) was boiled under reflux for 30 min. with 10% sodium hydroxide solution (30 ml.). An oil separated which solidified in the cold. Extraction with chloroform yielded a solid which separated from light petroleum (b. p. 60—80°) as colourless needles, m. p. 125° (Found, in material dried at 80° in high vacuum for 3 hr.: C, 79·35; H, 5·0. $C_{19}H_{14}ON_2$ requires C, 79·7; H, 4·9%). Light absorption in EtOH: max. at 270, 303, 308, 316, and 330 mμ (log ε 4·00, 3·77, 3·77, 3·93, and 3·76); min. at 295, 306, 312, and 322 mμ (log ε 3·63, 3·72, 3·73, and 3·74). The *picrate* separated from methanol as yellow needles, m. p. 189° with previous softening (Found: C, 56·8; H, 3·9. $C_{25}H_{17}O_8N_5,CH_4O$ requires C, 57·0; H, 3·8%).

Quinolino(1′ : 2′-3 : 4)iso*quinolino*(1″ : 2″-2 : 1)*glyoxalinium Series.—Quinolino*iso*quinolinoglyoxalinium perchlorate.* A solution of ωω-dibromoquinaldine (5·0 g.) in *iso*quinoline (40 ml.) was boiled under reflux for 4 hr. The mixture was cooled to about 30° and ether was added to prevent solidification of unused *iso*quinoline. Overnight dark crystals appeared and these were separated by decantation and well washed with ether. This solid was treated with charcoal in boiling water, to yield a clear yellow solution which deposited a red oil in the cold. The liquid was decanted from the oil, and sodium hydroxide solution was added until the solution was just alkaline to litmus. Several extractions with ether removed the liberated *iso*quinoline. The resulting solution was heated to expel ether and filtered.

To one-third of the filtrate excess of aqueous perchloric acid was added and the precipitated solid was collected, washed with water, and crystallised twice from methanol, to yield *quinolino*(1′ : 2′-3 : 4)iso*quinolino*(1″ : 2″-2 : 1)*glyoxalinium perchlorate* as pale yellow needles (Found: C, 61·8; H, 3·7. $C_{19}H_{13}O_4N_2Cl$ requires C, 61·9; H, 3·5%). Light absorption in EtOH: max. at 284, 295, 362, and 380 mμ (log ε 4·41, 4·36, 4·07, and 4·03); min. at 254, 292, 323, and 373 mμ (log ε 4·00, 4·34, 3·65, and 3·98).

To another third of the above filtrate was added aqueous hydrobromic acid until the solution was just acid to litmus, and then excess of hot aqueous picric acid. In the cold a yellow solid was precipitated which was separated, washed with water, and twice recrystallised from methanol to yield the *picrate* (0·80 g.) as yellow needles, m. p. 234° (Found: C, 60·0; H, 3·0. $C_{25}H_{15}O_7N_5$ requires C, 60·35; H, 3·0%).

*Action of sodium hydroxide on quinolino*iso*quinolinoglyoxalinium bromide.* To the remaining third of the above filtrate was added concentrated sodium hydroxide solution (to *ca.* 10% NaOH), and the mixture was boiled for 10 min. A white crystalline solid was produced and more separated in the cold. This solid was collected, dried, and crystallised twice from light petroleum (b. p. 60—80°) to yield colourless needles (1·1 g.), m. p. 138° (Found, in material dried at 110° in a high vacuum: C, 79·6; H, 5·1; N, 9·7. $C_{19}H_{14}ON_2$ requires C, 79·7; H, 4·9; N, 9·8%). The compound is hygroscopic. Light absorption in EtOH: max. at 234, 280, 303, 309, and 316·5 mμ (log ε 4·83, 4·13, 3·91, 3·83, and 3·98); min. at 256, 300, 307, and 312·5 mμ (log ε 3·83, 3·86, 3·81, and 3·80). The m. p. of the compound was unchanged on admixture with a sample of 2-2′-quinolylmethyl*iso*carbostyril synthesised as described below, and the ultraviolet and infrared spectra of the two were identical.

The action of aqueous sodium hydroxide on quinolino*iso*quinolinoglyoxalinium picrate yielded the same compound, m. p. 138°.

The *picrate* was prepared in methanol and recrystallised from acetone–ether as yellow needles, m. p. 214° (Found: C, 57·75; H, 3·4. $C_{25}H_{17}O_8N_5$ requires C, 58·25; H, 3·3%).

iso*Carbostyril acetate.* *iso*Quinoline *N*-oxide (5·8 g.) and acetic anhydride (100 ml.) were boiled under reflux for 5 hr. and the mixture was poured into ice and water. The brown crystals which separated (5·4 g.) were washed with water, dried, and recrystallised several times from light petroleum (b. p. 60—80°), to yield iso*carbostyril acetate* as colourless prismatic needles, m. p. 89° (Found: C, 70·9; H, 4·95. $C_{11}H_9O_2N$ requires C, 70·6; H, 4·8%). The mother-liquors of the above crystallisations yielded colourless needles of *iso*carbostyril produced by hydrolysis of some of the acetate when the reaction mixture was poured into water.

iso*Carbostyril.* *iso*Carbostyril acetate (1·0 g.) was dissolved in 10% aqueous hydrochloric acid (40 ml.) and the solution was kept at 80° for 30 min., cooled, and treated with solid sodium carbonate until alkaline. The precipitated solid was separated, washed with water, dried, and recrystallised from acetone, to yield *iso*carbostyril (0·40 g.) as colourless needles, m. p. 214°.

2-2′-*Quinolylmethyl*iso*carbostyril.* A solution of ω-bromoquinaldine (0·40 g.), *iso*carbostyril

(0·30 g.), and potassium hydroxide (0·1 g.) in methanol (25 ml.) was boiled under reflux for 2 hr., then poured into water, and the resulting white precipitate was collected, washed with water, dried, and recrystallised from light petroleum (b. p. 60—80°) to yield 2-2′-quinolylmethyl*iso*carbostyril (0·25 g.) as needles, m. p. 138° (Found: N, 9·7. Calc. for $C_{19}H_{14}ON_2$: N, 9·8%).

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, November 30th*, 1956.]

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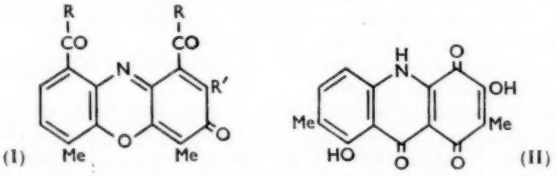
306. *Actinomycin. Part III.* The Reaction of Actinomycin with Alkali.*

By S. J. ANGYAL, E. BULLOCK, W. G. HANGER, W. C. HOWELL, and A. W. JOHNSON.

The production and purification of actinomycin B are described. Addition of dilute alkali to an alcoholic solution of actinomycin causes a marked hypsochromic effect which is reversible. The reaction obeys second-order kinetics and is interpreted as a fission of the oxygen bridge of the phenoxazin-3-one nucleus, giving rise to a highly strained and non-planar quinone anil. The reverse reaction involves two stages; ring closure and elimination of water. Isatin, another molecule which shows a hypsochromic shift in the spectrum after addition of alkali, is shown to possess spectral characteristics which differ from those of actinomycin in several respects.

ACTINOMYCIN B [1] has been prepared from strain "X-45" [2] and has been shown by chromatography [3] to consist of at least four components. Brockmann and Vohwinkel [4] have produced evidence to suggest that the chromophore is common to all members of the actinomycin group and consequently crystalline actinomycin B has been used for most of our degradative work aimed at the elucidation of the nature of the chromophore.

In a paper [5] describing its isolation and chemistry it was stated that actinomycin was probably a hydroxyquinone, on the basis of its reversible reduction and formation of acetyl and *leuco*-acetyl derivatives. This view was unchallenged until 1955 when, in a preliminary communication,[6] we pointed out that the absorption spectrum of actinomycin (max. at 234 and 444 mμ; log ε 4·50 and 4·33) was not of the usual hydroxyquinone type. The recent derivation of the 2-aminophenoxazin-3-one peptide structure (I; R′ = NH_2; R = L-threonyl-D-*allo*isoleucyl-L-prolylsarcosyl-L-*N*-methylvaline with the terminal carboxyl group esterified by the hydroxyl of the threonyl fragment) for actinomycin C_3 [7] has



(I) (II)

justified our earlier misgivings, although before this publication other chemical properties were discovered which were not in accord with the hydroxyquinonoid formulation. Thus,

* Part II, *J.*, 1952, 2672.

[1] Dalgliesh, Johnson, Todd, and Vining, *J.*, 1950, 2946.
[2] Lehr and Berger, *Arch. Biochem.*, 1949, **23**, 503.
[3] Brockmann and Gröne, *Naturwiss.*, 1953, **40**, 222, 224; 1954, **41**, 65; *Chem. Ber.*, 1954, **87**, 1036; Vining *et al.*, *Science*, 1954, **120**, 389; *J.*, 1956, 2469.
[4] Brockmann and Vohwinkel, *Naturwiss.*, 1954, **41**, 257.
[5] Waksman and Tishler, *J. Biol. Chem.*, 1942, **142**, 519.
[6] Angyal, Bullock, Hanger, and Johnson, *Chem. and Ind.*, 1955, 1295.
[7] Brockmann, Bohnsack, Franck, Gröne, Muxfeldt, and Süling, *Angew. Chem.*, 1956, **68**, 70.

the conversion of a hydroxyquinone into its anion usually involves a pronounced bathochromic shift in the absorption spectrum, whereas the initial yellow colour of a dilute solution of actinomycin in aqueous sodium hydroxide rapidly fades until an almost colourless solution (max. at 282—285, 343 and a low-intensity band at 458 mμ) is formed. Actinomycin can be recovered from the alkaline solution provided that it is not heated or even kept at room temperature for more than about one hour. After that, evolution of ammonia becomes pronounced and a neutral degradation product is produced, which on further reaction with alkali forms the salt of an acid. The product derived from actinomycin B with cold alkali described in our earlier paper [8] has now been shown to be a mixture of these compounds which can be separated by preliminary extraction of solutions in organic solvents with aqueous sodium hydrogen carbonate, followed by counter-current distribution in benzene–ethanol–water. In the actinomycin C series, the parallel substances have been investigated in detail by Brockmann and Franck.[9] The neutral

FIG. 1. *Rate of reaction of actinomycin with alkali calculated from* (a) *the rate of appearance of the* 343 mμ *peak* (×) *and* (b) *the rate of disappearance of the* 444 mμ *peak* (⊙).

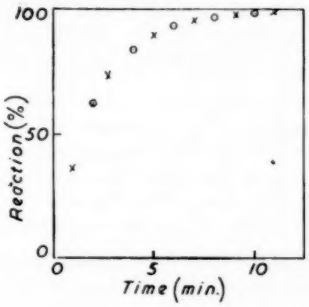
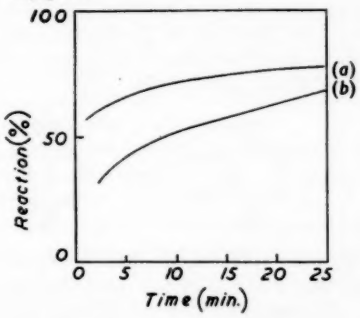


FIG. 2. *Rate of reaction of dilute acid with an alkaline solution of actinomycin calculated from* (a) *the rate of disappearance of the* 343 mμ *peak and* (b) *the rate of appearance of the* 444 mμ *peak.*



product, " deaminoactinomycin," was formed by acid hydrolysis of the 2-aminophenoxazin-3-one fragment (I; R = peptide; R′ = NH_2) to the corresponding 2-hydroxyphenoxazin-3-one (I; R = peptide; R′ = OH) and the acid degradation products, actinomycinic acid and the corresponding " deaminoactinomycinic acid " (NH_2 ⟶ OH), were formed by the opening of the peptide lactone groups with methanolic sodium hydroxide. Vigorous treatment of actinomycin with aqueous barium hydroxide causes extensive rearrangement, to give actinomycinol [8] or depeptidoactinomycin [10] (II).

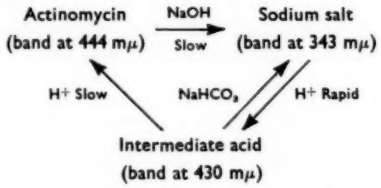
The alkaline decolorisation of actinomycin is not rapid, *e.g.*, under the experimental conditions used, decolorisation was complete only after about 30 minutes. The comparatively slow reaction enabled the kinetics to be determined by spectroscopic methods. It is of the second order, the rate being proportional to the concentration both of actinomycin and of alkali, and hence the decolorisation is not merely an ionisation but probably involves the addition of hydroxyl ion. The rate of disappearance of the band at 444 mμ is equal to the rate of appearance of the 343 mμ band (Figs. 1 and 2) and it is reasonable to conclude that no intermediate of appreciable stability is involved in the decolorisation process.

Reversal of the above reaction by acidification of the alkaline solution is not so straightforward; the 343 mμ band disappears much faster than the 444 mμ band appears and it

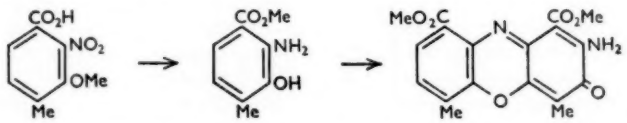
[8] Johnson, Todd, and Vining, *J.*, 1952, 2672.
[9] Brockmann and Franck, *Chem. Ber.*, 1954, **87**, 1767; *Angew. Chem.*, 1956, **68**, 68.
[10] Brockmann *et al.*, *Chem. Ber.*, 1956, **89**, 1373, 1379, 1393; see also Part V of this series, *J.*, in the press.

XUM

was not until this reaction was studied with a Cary self-recording spectrophotometer that the true state of affairs was established. It transpired that the 343 mμ band disappears immediately (within the limitations of the intrument) after acidification and is replaced by a band at 430 mμ with a shoulder at 445 mμ. This phase of the reaction is reversed when excess of aqueous sodium hydrogen carbonate is added to the freshly acidified solution, and in this respect the new product differs from actinomycin, solutions of which are unchanged by addition of sodium hydrogen carbonate. However, the solution of the product obtained by acidifying an alkaline solution of actinomycin is unstable and the spectrum slowly changes until that of the original actinomycin is obtained. The situation can therefore be represented :

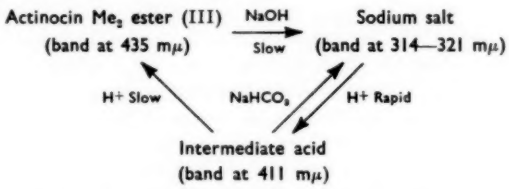


The same spectral changes are shown by deaminoactinomycin B and deaminoactinomycin acid (formed by prolonged reaction of actinomycin B with alkali) and also by actinocin dimethyl ester [11] (III), now synthesised by a modified procedure from 3-methoxy-2-nitro-*p*-toluic acid ($CO_2H = 1$) :



(III)

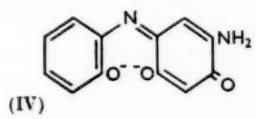
The ester (III) reacts more slowly with acid and alkali than does actinomycin, and the absorption maxima of the products are more widely spaced, so that it is easier to follow the various reactions by the spectral changes :

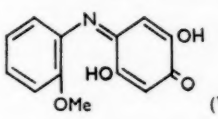


A similar cycle of reactions has been observed with dimethyl 2-amino-3-oxophenoxazine-1 : 9-dicarboxylate and it therefore appears that these reactions are characteristic of the phenoxazin-3-one nucleus. By contrast, acidification of solutions of sodium isatinate showed no immediate change in the spectrum; the strong peak at 370 mμ slowly faded, giving rise to the isatin peak at 415 mμ. The oxygen bridge in the phenoxazin-3-one system is part of a vinylogous ester system and it is probable that alkali causes a slow fission of the heterocyclic ring,[12] giving rise to an anion of a 2 : 2′-dihydroxyquinone anil. Quinone anils containing substituents in the 2- and/or 2′-position are known to be appreciably sterically hindered [13] and the consequent loss of planarity and inhibition of resonance has a marked effect on the absorption spectrum. In an attempt to prepare

[11] Brockmann and Muxfeldt, *Angew. Chem.*, 1956, **68**, 69.
[12] Cf. Butenandt, Biekert, and Neubert, *ibid.*, p. 379.
[13] McOmie and White, *J.*, 1955, 2619; Vittum and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 152; Horner and Sturm, *Chem. Ber.*, 1955, **88**, 329.

a crystalline derivative from the dianion (IV) an alkaline solution of 2-aminophenoxazin-3-one was treated with dimethyl sulphate and gave a red solid which was not obtained completely pure but appeared nevertheless to correspond to a molecular formula $C_{13}H_{11}O_4N$. The assigned structure (V) was derived from the dianion (IV) by replacement of the amino-group by hydroxyl and by methylation of the 2′-phenoxide group.


(IV)

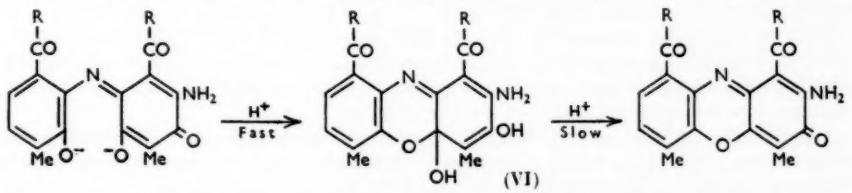

(V)

The spectrum of the ether (V) showed a marked qualitative resemblance to that of quinone anil [13] and the molecule must therefore have assumed a planar configuration, presumably by rotation about the nitrogen atom. By contrast, in the anion derived from actinomycin, the presence of bulky groups in all four positions *ortho* to the nitrogen bridge atom prevents rotation and thus contributes to the strong hypsochromic shift in the spectrum after the addition of alkali to actinomycin.

Acidification of the alkaline solution derived from actinomycin causes an immediate bathochromic shift of *ca.* 90 mμ and hence the product cannot be formulated as the acid corresponding to the anion. The intense band at 430 mμ in the spectrum of the acidification product suggests that the whole molecule is once more planar and examination of models suggests that this can be achieved only if the oxygen bridge is re-formed. This intermediate is tentatively formulated as (VI; R = peptide), a molecule which slowly reverts to the original phenoxazin-3-one structure by elimination of water.

The bathochromic shift of *ca.* 20 mμ observed when actinomycin is dissolved in acids [14] is attributed to salt formation on the heterocyclic nitrogen atom. The same phenomenon has been observed with xanthommatin, another substituted phenoxazin-3-one.[15]

Before it was appreciated that actinomycin was a derivative of phenoxazin-3-one, a number of other chromophoric systems reversibly decolorised by alkali, were considered. For example, this behaviour recalled certain hydroxy-derivatives of methylenequinones (*e.g.*, phenolphthalein with excess of alkali) but such compounds, unlike actinomycin, are not reversibly reduced unless other structural features are also present as in fuscin.[16] Another molecule which reproduces many of the properties of actinomycin including the reversible reduction is isatin which forms colourless salts of isatic acid on addition of alkali. When it was found [17] that 7-hydroxy-6-methylisatin, like actinomycin, could be

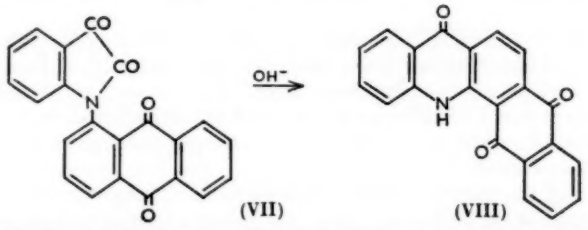

(VI)

converted into 7-methylbenzoxazolone-4-carboxylic acid (or the corresponding peptide) by oxidation with alkaline hydrogen peroxide, it seemed possible that isatin or a derived structure might be part of the actinomycin chromophore. The related structures indane-2 : 3-dione and coumaran-2 : 3-dione were eliminated because of the reported instability [18] and bathochromic spectral shift [19] with alkali respectively.

[14] See also Brockmann and Franck, *Naturwiss.*, 1954, **41**, 451.
[15] Butenandt, Scheidt, and Biekert, *Annalen*, 1954, **588**, 106.
[16] Barton and Hendrickson, *J.*, 1956, 1028.
[17] Bullock and Johnson, following paper.
[18] Perkin, Roberts, and Robinson, *J.*, 1912, **101**, 234.
[19] Cram, *J. Amer. Chem. Soc.*, 1950, **72**, 1028.

Little to distinguish actinomycin from the isatins could be derived from infrared spectra; thus chloroform solutions of actinomycin and isatin showed bands at 1754 cm.$^{-1}$ with inflections at 1770 cm.$^{-1}$ in the carbonyl region. In a polarographic examination of actinomycin B, kindly determined for us by Dr. N. S. Hush at the University of Manchester, a marked feature was the semiquinone formation in acid solution at 0·15 v. Isatin likewise showed this phenomenon at 0·28 v.[20] The formation of a purple anion from isatin [21] was also simulated when actinomycin was treated with alcoholic sodium ethoxide.

However, the ultraviolet and visible absorption spectrum of actinomycin showed appreciable differences from those of typical isatins. Thus, the intensity (log ε) of the



(VII) (VIII)

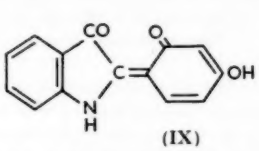
absorption band in the visible region of the spectrum rarely exceeded 3·0 for simple isatins whereas for actinomycin at 443—445 mμ it was 4·33. Treatment with dilute aqueous sodium hydroxide caused a hypsochromic effect (Δmμ) generally less (30—80 mμ) for the isatins than for actinomycin (98 mμ), and the intensity of the new band in the spectrum of the alkaline solution was greatly increased in the case of the isatins (Δ log ε 0·4—1·3) but unchanged for actinomycin. In some ways, this behaviour of actinomycin resembled more closely that of the *N*-acylisatins but these compounds, once converted into the isatic acids by treatment with alkali, did not re-form the parent acylisatins on acidification, possibly because of the competing quinoline formation.[22] Acidification of alkaline solutions of hydroxyisatins, unlike the case of actinomycin, caused an immediate ***hypsochromic*** effect, because of the neutralisation of the phenoxide ion, and this was followed by a slow bathochromic shift marking the appearance of the original isatin.

Nevertheless in view of the established acridone-quinone structure (II) for actinomycinol we were impressed by the alkaline rearrangement of *N*-(1-anthraquinonyl)isatin (VII) to 1 : 2-phthaloylacridone (VIII) [23] and it seemed that the carbon atoms of the quinonoid ring of actinomycinol must have been already present as a quinonoid ring.[24] Had this potential quinone ring been attached to the isatin group through the nitrogen atom as in (VII), the actinomycin chromophore on catalytic hydrogenation should have absorbed more hydrogen than the one mol. observed.[8] For this reason we attempted to prepare certain 3-oxindolylidene derivatives where the precursor of the quinone ring of actinomycinol was attached to the isatin through $C_{(3)}$.

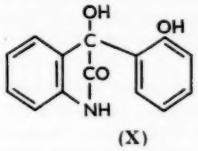
Friedlaender and his co-workers [25] have described several members of the corresponding indoxylylidene series (*e.g.*, IX or a tautomeric form) which they prepared by condensation of indoxyl, isatin α-chloride or α-anil with a variety of phenols. The products were reversibly reduced and addition of alkali caused a marked hypsochromic shift of the absorption spectrum. As with actinomycin, the colour of the original compound was restored immediately after acidification of the alkaline solution, suggesting that the reaction with alkali involved addition of a hydroxyl group rather than ring opening. We

[20] Sumpter, Williams, Wilkin, and Willoughby, *J. Org. Chem.*, 1949, **14**, 713.
[21] Sumpter, Wilkin, Williams, Wedemeyer, Boyer, and Hunt, *ibid.*, 1951, **16**, 1777.
[22] Jacobs, Winstein, Linden, Robson, Levy, and Seymour, *Org. Synth.*, Coll. Vol. III, 1955, p. 456.
[23] Bayer and Co., G.P. 286,095; *Chem. Zentr.*, 1915, II, 568.
[24] Cf. the formation of 2 : 5-dihydroxybenzoquinone from *apo*terramycin, Hochstein, Stevens, Conover, Regna, Pasternak, Gordon, Pilgrim, Brunings, and Woodward, *J. Amer. Chem. Soc.*, 1953, **75**, 5455.
[25] Friedlaender *et al.*, *Monatsh.*, 1908, **29**, 375, 387, and later papers.

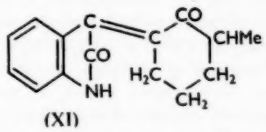
were unable, however, to obtain corresponding compounds of the oxindolylidene series from similar condensations using *N*-methyloxindole, isatin β-dichloride, β-anil, β-*p*-



(IX)



(X)



(XI)

methylanil,[26] or β-*p*-nitroanil. In another approach isatins were treated with the Grignard derivatives of *o*-methoxyaryl halides [27] and the products demethylated to yield 3-*o*-hydroxyaryldioxindoles, *e.g.*, (X), but in spite of numerous attempts these compounds could not be dehydrated. The 3-*o*-methoxyaryldioxindoles were also reduced to the corresponding oxindoles with stannous chloride,[28] and the methoxy-groups were hydrolysed, but in all the cases investigated the colourless phenolic products resisted purification and, as they clearly did not possess the required oxindolylidene structures, this approach was abandoned. In other experiments, 2-3′-dioxindolyl-6-methyl*cyclo*hexanone was dehydrated to 2-methyl-6-3′-oxindolylidene*cyclo*hexanone [29] (XI), but attempted dehydrogenation with selenium dioxide failed to give a coloured product.

All this evidence, coupled with the fact that actinomycin, unlike isatin, failed to react with *o*-phenylenediamine or thioindoxyl,[30] led us to abandon structures for actinomycin based on the isatin chromophore.

Experimental

95% Ethanol was used as the solvent in determinations of absorption spectra, and infrared spectra were determined on mulls in Nujol except where otherwise stated.

Production of Actinomycin B (with Messrs. R. Elsworth, J. W. S. Ford, R. Harris-Smith, and V. Williams, of the Ministry of Supply Microbiological Research Station, Porton).—Sub-cultures of strain X-45 [2] were prepared on tomato-agar slopes. After inoculation these were incubated at 25° for 4 days in 1 oz. screw-capped bottles with the caps loosened. They were stored in a refrigerator with the caps tightened, and the sub-cultures were renewed at monthly intervals. The medium was prepared from glucose (10 g.), peptone (1 g.), homogenised canned tomato (20 g.), dipotassium hydrogen phosphate (1 g.), calcium carbonate (2 g.), and agar (15 g.) in tap-water (to 1 l.), and if necessary the pH was adjusted to 7·0 with 5N-potassium hydroxide.

Primary seeds were prepared by inoculation from a slope into the medium (80 c.c.) in a 40 oz. narrow-necked screw-capped bottle. It was shaken (98 strokes/min.; 2″ amplitude) for 48 hr. at 25° after which there was a nodular deposit on the walls of the bottle and a diffuse growth in the medium. The primary seed medium was prepared from dextrin (10 g.), maize-steep liquor (5 c.c.), and dipotassium hydrogen phosphate (1 g.) in distilled water (to 1 l.). The pH was adjusted to 6·5 with 5N-potassium hydroxide as before, and calcium carbonate (5 g.) was added.

Secondary seeds were prepared by transferring the primary seed growth described above into a 20-l. aspirator containing the main culture medium. The contents were incubated at 25° for 48 hr. with thorough aeration (30 l./min.) to produce an evenly dispersed nodular growth. The main culture was grown at 25° in 80-l. batches after inoculation with the secondary seed (8 l.) until the yield of actinomycin reached a maximum (*ca.* 7 days). The main culture solution was prepared from peptone (Evans; 1% w/v), maize-steep liquor (0·5% w/v), brown sugar (2% w/v), lard oil (edible grade; 0·3% w/v), and dipotassium hydrogen phosphate (0·1% w/v) at a pH of 6·0—7·0 adjusted before sterilisation.

Most of the actinomycin was in the mycelium and consequently the liquid phase was rejected. Hyflo Supercel (0·625%) was added to the broth, and the mycelium separated in the centrifuge.

[26] Pummerer and Goettler, *Ber.*, 1910, **43**, 1381.
[27] Inagaki, *J. Pharm. Soc. Japan*, 1939, **59**, 5.
[28] Marschalk, *Bull. Soc. chim. France*, 1952, 949.
[29] Cf. Braude and Lindwall, *J. Amer. Chem. Soc.*, 1933, **55**, 325.
[30] Harley-Mason, *J.*, 1942, 404.

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The wet mycelium was extracted in ½-gallon bottles with 95% ethanol (3·3 l. per kg.). After mixing, the bottle was kept overnight, shaken for 2 hr., heated at 60° for 1 hr. on the water-bath, and again shaken for 2 hr. The solids were separated and the alcoholic solution (containing *ca.* 33% of the total amount of actinomycin produced) used in the next stage of the purification. By a modified cylinder-plate method of microbiological assay,[31] the production was subjected to analytical control at all stages.

Isolation of Actinomycin B.—Removal of the solvent from the aqueous-alcoholic extract (60 l.) as prepared above, at 30° *in vacuo*, yielded a thick orange emulsion (5 l.) which was repeatedly extracted with benzene (6 × 500 c.c.). Removal of the solvent from the combined benzene extracts gave a deep red semi-solid gel (300 g.). Addition of ether (2 l.) precipitated the actinomycin as a sticky orange solid which, after repeated washing with ether (10 × 100 c.c.) and drying, gave an orange solid (25 g.). Evaporation of the ethereal filtrates gave a deep red residue which was treated with light petroleum (b. p. 60—80°; 2 l.), a further quantity of crude actinomycin being precipitated. After another treatment with light petroleum, nearly all of the actinomycin was obtained free from lard oil and other fatty substances present in the mycelium. Crystalline actinomycin B was obtained as bright red prisms, m. p. 250—253°, from the combined solids (40 g.) by crystallisation from ethanol. As actinomycin was sparingly soluble in ethanol, it was preferable to dissolve the solid in chloroform, then to add excess of ethanol and remove most of the chloroform by evaporation.

The product was examined by paper chromatography on Whatman No. 1 paper which had been soaked in 4% aqueous sodium naphthalene-2-sulphonate [3] and dried between other sheets of filter paper. The actinomycin was applied to the paper as a benzene solution, and the chromatogram developed with pentyl acetate which had been equilibrated with the sodium naphthalene-2-sulphonate solution. By this means the product was shown to contain four coloured substances, of R_F 0·74, 0·38, 0·10, and 0·03, which were estimated to occur in the following approximate proportions: 80—90, 10, 5, and <1% respectively.

Chromatographic Separation of the Actinomycin B Complex.—Activated alumina (100 g.) was warmed with aqueous 10% acetic acid (100 c.c.) at 70° on the water-bath for 2 hr. with constant stirring. The alumina was separated and washed with hot distilled water until the pH of the filtrate was 4—5. It was then suspended in methanol for 20 min., separated, washed with methanol, and dried at room temperature for 24 hr. This alumina has a low capacity and only small quantities of actinomycin could be separated at a time.

Actinomycin B complex (20 mg.) was applied to a column of alumina (15 × 1 cm.), and the sharp, uppermost, orange-red band developed with gradually increasing concentrations of chloroform in benzene. The process of the separation was followed by chromatography on paper as above but the early fractions contained only the actinomycin with R_F 0·74 which was followed by the component of R_F 0·38 and finally that of R_F 0·10. The pure actinomycin, R_F 0·74, was recrystallised from ethanol. Light absorption: max. at 232—236 and 443—445 mμ (log ε 4·50 and 4·33). Infrared absorption: max. at 3340, 3250, 1750, 1652, 1588, 1515, 1315, 1300, 1270, 1190, 1100, 1075, 1055, 1010, 980, 950, 875, and 760 cm.$^{-1}$. Determinations (i) in hexachlorobutadiene showed additional max. at 2940, 1407, and 1360 cm.$^{-1}$ and (ii) in chloroform at 1635 cm.$^{-1}$.

Reaction of Actinomycin with Alkali.—Aqueous 2·5N-sodium hydroxide (0·1 c.c.) was added to a 50% aqueous-ethanolic solution (5 c.c.) of actinomycin, the concentration of which (3 mg. actinomycin in 50 c.c.) was suitable for spectroscopic examination. Light absorption: max. at 285, 344, and 458 mμ (log ε 4·13, 4·38, and 3·05 respectively). The changes in intensity at 344 and 444 mμ were recorded and the results plotted (Fig. 1).

Further runs were made by adding varying amounts of aqueous sodium hydroxide to the actinomycin solution (2·5 c.c. as above): (i) 0·1N-NaOH (0·3 c.c.) + H_2O (0·4 c.c.); (ii) 0·1N-NaOH (0·5 c.c.) + H_2O (0·2 c.c.); and (iii) 0·1N-NaOH (0·7 c.c.): the calculated half-lives in the three cases were 8·3, 5, and 3·75 min. respectively, *i.e.*, proportional to the concentration of sodium hydroxide.

Acidification of an Alkaline Solution of Actinomycin.—A solution (2·5 c.c.) of actinomycin in 50% ethanol (as in the previous experiment) was mixed with 0·1N-aqueous sodium hydroxide (0·3 c.c.) and kept for 4·5 hr. It was then diluted to twice its original volume, 0·3N-hydrochloric acid (0·1 c.c.) was added, and spectral readings were taken as before. The results are plotted in Fig. 2.

[31] Brownlee, Delves, Dorman, Green, Grenfell, Johnson, and Smith, *J. Gen. Microbiol.*, 1938, **2**, 40.

*3-Hydroxy-2-nitro-*p*-toluic Acid* (CO_2H = 1).—3-Methoxy-2-nitro-*p*-toluic acid (7·6 g.; prepared by methylation [32] and subsequent nitration [33] of 3-hydroxy-*p*-toluic acid [34]) and freshly prepared pyridine hydrochloride (22 g.) were heated in an oil-bath at 190—200° for 45 min. The cooled mixture was poured into water (200 c.c.) and extracted with ether (3 × 100 c.c.). The combined ethereal extracts were washed and dried, the solvent was removed, and the residue crystallised from water, to give the *product* as lemon-yellow needles, m. p. 185·5—186·5° (6·7 g., 94%) (Found, on a sample sublimed at 140°/0·05 mm.: C, 48·9; H, 3·5; N, 7·5. $C_8H_7O_5N$ requires C, 48·7; H, 3·6; N, 7·1%).

*Methyl 3-Hydroxy-2-nitro-*p*-toluate.*—A mixture of 3-hydroxy-2-nitro-*p*-toluic acid (6·6 g.), methanol (4·1 c.c.), ethylene dichloride (10 c.c.), and concentrated sulphuric acid (0·5 c.c.) was heated under reflux for 24 hr. After cooling, the mixture was diluted with water (100 c.c.) and extracted with ether (3 × 100 c.c.). The combined ethereal extracts were washed with water and dried and the solvent was removed to give the crude *ester* (7·1 g.) which crystallised from aqueous methanol in needles (5·35 g., 76%), m. p. 116—116·5°. The mixture of ester and unchanged acid from the mother-liquors can be re-esterified. For analysis a sample was sublimed at 90°/0·05 mm. (Found: C, 51·4; H, 4·1; N, 6·9. $C_9H_9O_5N$ requires C, 51·2; H, 4·3; N, 6·6%).

Methyl 3-Hydroxy-4-methylanthranilate Hydrochloride.—The foregoing nitro-ester (2·76 g.) was hydrogenated in absolute ethanol (35 c.c.) and at room temperature and pressure over Raney nickel (*ca.* 1 g.). The catalyst was separated and the product isolated as its hydrochloride by dilution of the filtrate with ether (200 c.c.) and saturation of the filtrate with dry hydrogen chloride. The *product* (2·65 g., 93%) was obtained as colourless needles, m. p. 168—170° (decomp.) after two recrystallisations from ethanol–ether (Found: C, 49·7; H, 5·3; Cl, 15·9. $C_9H_{11}O_3N$,HCl requires C, 49·7; H, 5·55; Cl, 16·3%).

Dimethyl 2-Amino-4:6-dimethyl-3-oxophenoxazine-1:9-dicarboxylate (*Actinocin Dimethyl Ester*).—A solution of methyl 3-hydroxy-4-methylanthranilate hydrochloride (2·5 g.) in phosphate buffer (3 l.; pH 7·1) was kept at 40—45° while a solution of potassium ferricyanide (7·65 g.) in water (300 c.c.) was added dropwise with stirring. After cooling, the product (1·52 g., 74%) which had formed as a bright orange flocculent precipitate, was separated, washed, and dried. Crystallisation from ethyl acetate or benzene gave *actinocin dimethyl ester* as fine orange needles, decomp. 195—198° (Found: C, 60·9; H, 4·4; N, 7·9. $C_{18}H_{14}O_6N_2$ requires C, 60·7; H, 4·5; N, 7·9%). Light absorption: (i) max. at 240 and 435 mμ (log ε 4·57 and 4·49 respectively); (ii) in 1:1-aqueous-ethanolic 0·05N-NaOH: max. at 316 and 445 mμ (log ε 4·25 and 3·62).

3-Hydroxy-2-nitrobenzoic Acid.—3-Methoxy-2-nitrobenzoic acid [35] (1 g.) was fused with freshly prepared pyridine hydrochloride (2·5 g.) at 220° (oil-bath) for 40 min. The cooled melt was treated with water (20 c.c.) and cooled in ice. The brown precipitate was separated (0·9 g.) and crystallised from water, then having m. p. 172—174° (Hegedus [36] gives m. p. 176—178°); it was used directly for the next stage.

Methyl 3-Hydroxy-2-nitrobenzoate.—The foregoing acid (0·9 g.) was heated under reflux with dry methanol (2 c.c.), ethylene dichloride (20 c.c.), and concentrated sulphuric acid (3 drops) for 24 hr. The resulting solution was washed with water, and the solvent removed *in vacuo*. The methyl ester was thus obtained as white needles, m. p. 108—110° (lit.,[37] 115°) after crystallisation from water.

Dimethyl 2-Amino-3-oxophenoxazine-1:9-dicarboxylate.—Methyl 3-hydroxy-2-nitrobenzoate (1·5 g.) was hydrogenated in ethanol (40 c.c.) over Raney nickel (1 g.) at room temperature and pressure. Three mols. of hydrogen were absorbed in 4 hr., then the catalyst was separated and the filtrate diluted with ether (100 c.c.). The solution was treated with dry hydrogen chloride for 1½ hr. and the white hydrochloride (1·3 g.), m. p. 197° (decomp.), of methyl 3-hydroxyanthranilate which was formed was separated. The hydrochloride (1·2 g.) was heated in a phosphate buffer (3 l.; pH 7·4) to 40°. A solution of potassium ferricyanide (4·5 g.) in water (300 c.c.) was added slowly with stirring, then the product was cooled and the pale orange

[32] Perkin and Weizmann, *J.*, 1906, **89**, 1658.
[33] Simonsen and Rau, *J.*, 1921, **119**, 1339.
[34] Meldrum and Perkin, *J.*, 1908, **93**, 1416.
[35] Nyc and Mitchell, *J. Amer. Chem. Soc.*, 1948, **70**, 1847.
[36] Hegedus, *Helv. Chim. Acta*, 1951, **34**, 611.
[37] Senoh, Seki, and Kikkawa, *J. Chem. Soc. Japan*, 1953, **74**, 251.

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crystalline *product* (0·8 g.) separated. After crystallisation from chloroform–ethyl acetate it formed orange needles, m. p. 225—226° (decomp.) (Found: C, 58·64; H, 3·7; N, 8·5. $C_{16}H_{12}O_6N_2$ requires C, 58·55; H, 3·7; N, 8·5%), readily soluble in polar organic solvents but only slightly soluble in water. Light absorption: (i) max. at 237 and 433 mμ (log ε 4·51 and 4·43); (ii) in 95% EtOH–10% aqueous NaOH (1 : 1): max. at 318 and 468 mμ (log ε 4·26 and 3·45); (iii) in 95% ethanol–10N-hydrochloric acid (1 : 4): max. at 231, 468, and 500 mμ (log ε 4·63, 4·45, and 4·38 respectively).

Methylation of an Alkaline Solution of 2-Aminophenoxazin-3-one.—2-Aminophenoxazin-3-one was prepared according to Zincke and Hebebrand,[38] forming very dark needles, m. p. 245° (decomp.) (from benzene). Light absorption: max. at 236 and 432 mμ (log ε 4·34 and 4·21).

The amino-compound (500 mg.) was dissolved in dioxan (50 c.c.) and diluted with water (50 c.c.). Aqueous 2·5N-sodium hydroxide (30 c.c.) was added, the solution kept for 30 min., and the precipitated 2-aminophenoxazin-3-one (280 mg.) separated. The alkaline solution was treated at room temperature with a large excess of dimethyl sulphate (7·8 g.) in six portions, during 2 hr. with constant shaking. Aqueous ammonia (3 c.c.; *d* 0·88) was added to decompose the excess of dimethyl sulphate, and the solution then acidified with hydrochloric acid to pH 3. After dilution with water (100 c.c.), the product was extracted with chloroform (3 × 100 c.c.), and the combined extracts were washed and dried. Removal of the solvent under reduced pressure gave a red gum which was treated with aqueous 2·5N-sodium hydroxide (10 c.c.) and any insoluble material separated. The alkaline solution was carefully acidified and the dark red precipitate removed, washed with water, and dried *in vacuo*. The product (70 mg.), m. p. 77° (decomp.), could not be crystallised satisfactorily (Found: C, 63·0; H, 5·1; N, 5·5; OMe, 9·0. Calc. for $C_{13}H_{11}O_4N$: C, 63·6; H, 4·5; N, 5·7; 1OMe, 12·6%). It was very soluble in polar organic solvents and only slightly soluble in water. It dissolved in aqueous sodium hydrogen carbonate solution with liberation of carbon dioxide. Light absorption: max. at 502, 306, 283, and 219 mμ (log ε 3·36, 3·93, 3·97, and 4·14 respectively).

5-Hydroxy-2-indoxylylidenecyclohexa-3 : 5-dienone [25] (*from Ethanol*).—The product obtained from the condensation of isatin-α-chloride and resorcinol formed thick, almost black needles with a green reflex. Light absorption: (i) max. at 229, 288, and 518 mμ (log ε 3·24, 3·39, and 3·90 respectively); (ii) in EtOH–0·1N-aqueous sodium hydroxide (1 : 1), max. at 225 and 327 mμ (log ε 3·44 and 4·18 respectively).

Reaction of Isatin with Arylmagnesium Bromides.—Magnesium (0·9 g., 1·5 mol.; previously etched with 1% nitric acid for 2 min., then washed and dried), ethyl bromide (2 drops), and dry ether (10 c.c.) were heated under reflux until the reaction had ceased. The aryl bromide (0·5 g.) was added, the mixture again heated, and a solution of the remainder of the aryl bromide (4·7—5·8 g., 1 mol.) in ether (50 c.c.) added slowly. The solution was heated under reflux for 3 hr., then isatin (1·5 g., 1 mol.) was gradually introduced by means of a Soxhlet extractor (6—8 hr.). The product was poured into cold 10% sulphuric acid (300 c.c.), unchanged isatin being precipitated and removed. The ethereal layer was separated and the aqueous solution again extracted with ether. The combined ethereal extract was washed and dried, the solvent removed, and the colourless crystalline residue recrystallised. Yields were of the order of 30%. Thus were prepared:

3-o-*Methoxyphenyldioxindole* (1·0 g.), colourless needles, m. p. 238°, from aqueous ethanol (Found: C, 70·6; H, 5·1; N, 5·5. $C_{15}H_{13}O_3N$ requires C, 70·6; H, 5·1; N, 5·5%). The product could be readily purified by sublimation *in vacuo*.

3-p-*Methoxyphenyldioxindole* (1·2 g.), colourless needles, m. p. 180° (from ethanol) (Found: N, 5·55%).

3-(2 : 4-*Dimethoxy*-m-*tolyl*)*dioxindole* (0·6 g.) [from 3-bromo-2 : 6-dimethoxytoluene (see below)], needles, m. p. 227° (decomp.), from aqueous methanol (Found: C, 68·1; H, 5·7; N, 4·7. $C_{17}H_{17}O_4N$ requires C, 68·2; H, 5·7; N, 4·7%). The product was also purified by sublimation at 170°/0·1 mm.

3-Bromo-2 : 6-dimethoxytoluene.—2 : 6-Dimethoxytoluene (20 g.) in chloroform (75 c.c.) was treated with bromine (23 g.) in chloroform (75 c.c.), and the chloroform then removed by distillation. The residual brown oil (34 g.) was distilled through a short Vigreux column to give the *bromo-derivative*, b. p. 147—149°/15 mm. (Found: Br, 33·1. $C_9H_{11}O_2Br$ requires Br, 33·4%).

[38] Zincke and Hebebrand, *Annalen*, 1882, **226**, 61.

3-o-*Methoxyphenyloxindole*.—3-(*o*-Methoxyphenyl)dioxindole (0·5 g.) was dissolved in glacial acetic acid (10 c.c.), a solution of stannous chloride (1 g.) in acetic acid (20 c.c.) and concentrated hydrochloric acid (1 c.c.) was added, and the mixture heated on the water-bath at 80—90° for 10 min. The product was poured into water (150 c.c.), giving white needles of 3-(o-*methoxyphenyl*)*oxindole* (300 mg.), m. p. 148° (from aqueous ethanol) (Found : C, 75·4; H, 5·55; N, 5·85. $C_{15}H_{13}O_2N$ requires C, 75·3; H, 5·5; N, 5·85%).

3-p-*Methoxyphenyloxindole*.—Prepared from 3-*p*-methoxyphenyldioxindole (500 mg.) by a method similar to the foregoing, this *product* (400 mg.) formed colourless crystals, m. p. 163—165° (decomp.), from aqueous ethanol (Found, in a sample sublimed under reduced pressure : C, 75·4; H, 5·7; N, 5·8%). Light absorption (in *NN*-dimethylformamide) : log $\varepsilon_{max.}$ 4·42 at 259 mμ.

3-(2 : 4-*Dimethoxy*-m-*tolyl*)*oxindole*.—Prepared by reduction of the corresponding dioxindole derivative as above, this *product* (240 mg.) was obtained as colourless crystals, m. p. 162°, which after crystallisation from aqueous ethanol could be sublimed under reduced pressure (Found : N, 4·85. $C_{17}H_{17}O_3N$ requires N, 4·95%). Light absorption (in *NN*-dimethylformamide) : log $\varepsilon_{max.}$ 4·19 at 268 mμ.

Isatin β-p-*Nitroanil*.—Isatin (5 g.) in ethanol (150 c.c.) was heated with an alcoholic solution of *p*-nitraniline (5 g.) under reflux for 7 hr. and, on cooling, the *product* (8 g.) crystallised as red needles, m. p. 159° (Found, on a sample sublimed at 130°/0·1 mm. : C, 63·0; H, 3·3; N, 15·9. $C_{14}H_9O_3N_3$ requires C, 62·9; H, 3·4; N, 15·7%).

2-(3-*Dioxindolyl*)-6-*methyl*cyclo*hexanone*.—Isatin (5 g.), 2-methyl*cyclo*hexanone (3·9 g.), and piperidine (2 g.) were dissolved in dry dioxan and kept at room temperature for 24 hr. A small quantity of 3 : 3-dipiperidino-oxindole which separated was removed; when the filtrate was diluted with water (150 c.c.) a further quantity of the dipiperidino-oxindole was obtained, and again separated. After being kept a week, the *product* (2·3 g.) separated from the solution as colourless prisms, m. p. 168° (decomp.) after crystallisation from aqueous ethanol (Found : C, 69·1; H, 6·4; N, 5·4. $C_{15}H_{17}O_3N$ requires C, 69·5; H, 6·6; N, 5·4%).

2-*Methyl*-6-3′-*oxindolylidene*cyclo*hexanone*.—2-(3-Dioxindolyl)-6-methyl*cyclo*hexanone (1 g.) was suspended in ethanol (2 c.c.) and concentrated hydrochloric acid (0·5 c.c.) was added. The mixture was warmed, a clear orange solution being formed which slowly deposited the dehydration *product* as orange prisms (0·8 g.), m. p. 142° (from aqueous ethanol) (Found : C, 74·7; H, 6·1; N, 6·0. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·2; N, 5·8%).

Absorption Spectra of Substituted Isatins.—Spectra of the following isatin derivatives were determined in (i) 95% ethanol and (ii) 95% ethanol–0·1N-aqueous sodium hydroxide (1 : 1).

5-*Hydroxy*- :[39] (i) max. at 482—485, 302, 256, and 214 mμ (log ε 2·95, 3·34, 4·27, and 3·99 respectively); (ii) max. at 422—424 and 248 mμ (log ε 3·52 and 4·16 respectively).

5-*Methoxy*- :[40] (i) max. at 472—475, 300, 254, and 214 mμ (log ε 2·84, 3·29, 4·32, and 4·09 respectively); (ii) max. at 391—394 and 233—224 mμ (log ε 3·61 and 4·17 respectively).

1-*Acetyl*-5-*methoxy*- : (i) max. at 374—375 and 238—240 mμ (log ε 3·06 and 4·08); (ii) max. at 325, 258—260, and 228—230 mμ (log ε 3·30, 3·85, and 4·18 respectively).

7-*Methoxy*-1-*methyl*- :[41] (i) max. at 462—467, 322, and 228 mμ (log ε 2·94, 3·48, and 4·26 respectively); (ii) max. at 393, 278, and 238 mμ (log ε 3·56, 3·44, and 4·28 respectively).

1-*Benzyl*- : (i) max. at 421—425, 298, 251, and 245 mμ (log ε 2·67, 3·37, 4·23, and 4·30 respectively); (ii) max. at 390, 268, and 230 mμ (log ε 3·78, 3·87, and 4·27 respectively).

1-*Phenyl*- : (i) max. at 419—422 and 244 mμ (log ε 2·56 and 4·36 respectively); (ii) max. at 398, 282, 253, and 228 mμ (log ε 3·87, 3·95, 4·16, and 4·17 respectively).

1-*Acetyl-isatin* :[22] (i) max. at 341—343, 272, 265, and 236 mμ (log ε 3·56, 3·91, 3·91, and 4·36 respectively); (ii) max. at 326, 264, and 231 mμ (log ε 3·47, 3·99, and 4·29 respectively).

Isatin and 1-methylisatin : see Ault, Hirst, and Morton.[42]

The award of a Nuffield Dominion Travelling Fellowship (to S. J. A.), a Ramsay Memorial Fellowship and a New Zealand Postgraduate Scholarship (to W. G. H.), a Postdoctoral Overseas Fellowship of the National Research Council of Canada (to W. C. H.), and a D.S.I.R. maintenance grant (to E. B.) are gratefully acknowledged. We are also indebted to Dr. D. W.

[39] Hartmann and Panizzon, *Helv. Chim. Acta*, 1936, **19**, 1327.
[40] Bachmann and Picha, *J. Amer. Chem. Soc.*, 1946, **68**, 1601.
[41] Cook, Loudon, and McCloskey, *J.*, 1952, 3904. We are very grateful to Dr. Loudon for the gift of a sample of this compound.
[42] Ault, Hirst, and Morton, *J.*, 1935, 1653.

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Henderson and Mr. R. Elsworth and their colleagues of the Ministry of Supply Microbiological Station, Porton, for their help in producing actinomycin B concentrate, and to Professor Sir Alexander Todd, F.R.S., for his interest and encouragement.

DEPARTMENT OF CHEMISTRY, THE UNIVERSITY, NOTTINGHAM.
THE UNIVERSITY CHEMICAL LABORATORIES, CAMBRIDGE. [*Received, September* 13*th*, 1956.]

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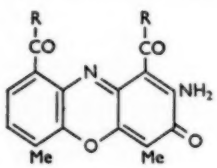
307. *Actinomycin. Part IV.* An Oxidative Degradation of Actinomycin B.*

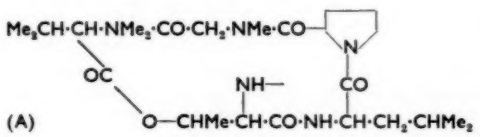
By E. BULLOCK and A. W. JOHNSON.

Oxidation of actinomycin B with alkaline hydrogen peroxide gives an acidic peptide of 7-methylbenzoxazolone-4-carboxylic acid. The lactone of the peptide group of actinomycin is hydrolysed during the oxidation but all of the original amino-acids are retained. Acid hydrolysis of the oxidation product gives 7-methylbenzoxazolone-4-carboxylic acid, the structure of which is confirmed by synthesis.

As a result of an extensive and elegant series of degradative experiments, Brockmann and his colleagues [1] have deduced structure (I) for actinomycin C_3, where R = L-threonyl-D-*allo*isoleucyl-L-prolyl-sarcosyl-L-*N*-methylvaline with the terminal carboxyl group esterified by the hydroxyl group of the threonyl fragment, as in (A). The chemistry of the actinomycins [2] as well as the rather confused nomenclature of the group [3] have been reviewed recently. The chemical differences between the various actinomycins involve the nature and order of the amino-acids in the peptide chains; the phenoxazin-3-one nucleus seems



(I)



(A)

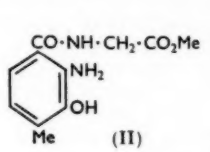
to be common to all the actinomycins so far examined.[4] It is of particular interest that the actinomycins can arise from the oxidative condensation of peptides derived from 3-hydroxy-4-methylanthranilic acid and that this reaction has been achieved *in vitro* by the aerial oxidation of a solution of *N*-(3-hydroxy-4-methylanthraniloyl)glycine methyl ester (II) in aqueous ammonium carbonate,[4] to give (I; R = $NH{\cdot}CH_2{\cdot}CO_2Me$), a reaction which recalls the formation of the insect pigment xanthommatin (III) by a similar oxidation of 3-hydroxykynurenine.[5]

Our own work on actinomycins B [6] and D [7] gives further support to formulæ of the type (I). Thus, from the action of alkaline hydrogen peroxide on actinomycin B we have obtained a colourless crystalline acid, $C_{32}H_{44}O_{10}N_6,2H_2O$ which has been purified by counter-current distribution between ethyl acetate and a phosphate buffer at pH 5·9. This acid still contained all five of the constituent amino-acids, L-*N*-methylvaline, sarcosine, L-proline, D-valine, and L-threonine, of the original actinomycin B peptide chains.

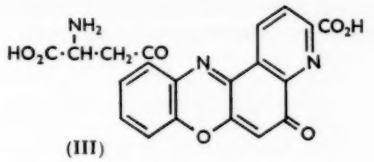
* Part III, preceding paper.

[1] Brockmann, Bohnsack, Franck, Gröne, Muxfeldt, and Süling, *Angew. Chem.*, 1956, **68**, 70.
[2] Johnson, Chem. Soc. Special Publ., No. 5, 1956, 82.
[3] Roussos and Vining, *J.*, 1956, 2469.
[4] Brockmann and Muxfeldt, *Angew. Chem.*, 1956, **68**, 69.
[5] Butenandt, Schiedt, Biekert, and Cromartie, *Annalen*, 1954, **588**, 106; 1955, **590**, 75.
[6] Dalgliesh, Johnson, Todd, and Vining, *J.*, 1950, 2946.
[7] Vining and Waksman, *Science*, 1954, **120**, 389.

Potentiometric titration of the acid revealed the presence of only one carboxyl group and the above molecular formula was supported by determinations of the equivalent. The ultraviolet absorption spectrum suggested the presence of a benzenoid ring and the

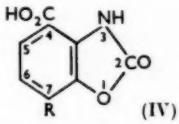


(II)

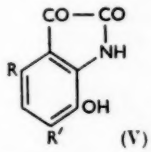


(III)

resemblance of the spectrum to those of 3-hydroxyanthranilic acid and its derivatives [8] was especially striking. The infrared spectrum of the product as a mull in Nujol showed a band in the carbonyl region at 1786 cm.$^{-1}$ which is generally associated with the presence of a $\beta\gamma$-unsaturated five-membered lactone,[9] and, combining all of the foregoing evidence, it seemed that the degradation product might well be a peptide derived from benzoxazolone-4-carboxylic acid (IV; R = H).



(IV)



(V)

This was confirmed by acid hydrolysis of the peptide, the amino-acids being removed and another crystalline carboxylic acid, $C_9H_7O_4N$, obtained, the ultraviolet absorption of which closely resembled that of the parent peptide. This product contained no free hydroxyl or amino-group, but the presence of a $\beta\gamma$-unsaturated five-membered lactone was again suggested by the band at 1799 cm.$^{-1}$ in the infrared spectrum of a chloroform solution. Bands at 1145, 1087, 1038, 971, and 810 cm.$^{-1}$ were consistent with the presence of two adjacent hydrogen atoms in the benzene nucleus; bands between 900 and 860 cm.$^{-1}$ usually associated with isolated hydrogen atoms on a benzene ring were absent.[10] The acid was therefore formulated as either 7- (IV; R = Me) or 5-methylbenzoxazolone-4-carboxylic acid, and a decision in favour of the 7-methyl isomer was reached after each isomer had been synthesised. Application of the Sandmeyer synthesis [11] to 2-(and 6-)methoxy-*m*-toluidine ($NH_2 = 1$) gave 7-methoxy-6-(and 4-[12])methylisatin which was hydrolysed to the corresponding 7-hydroxy-6-(and 4-)methylisatin (V; R = H, R′ = Me, and *vice versa*, respectively). Oxidation of the 7-hydroxyisatins with alkaline hydrogen peroxide gave the 7- and 5-methylbenzoxazolone-4-carboxylic acids, presumably with intermediate formation of a labile carbamic acid.[13]

The formation of a benzoxazolone on oxidation of a phenoxazin-3-one was rather unexpected and for a time led us to believe that actinomycin was a derivative of isatin (see Part III, preceding paper). However, the reaction appears to be fairly general, as shown by the isolation of benzoxazolone itself from a similar oxidation of 2-aminophenoxazin-3-one (VI). Very recently, Butenandt, Biekert, and Neubert [14] reported the formation of 4-acetylbenzoxazolone on oxidation of 1 : 8-diacetyl-2-aminophenoxazin-3-one with chromic acid.

Besides the benzoxazolone peptide, the other major product from the reaction of

[8] Nyc and Mitchell, *J. Amer. Chem. Soc.*, 1948, **70**, 1847.
[9] Grove and Willis, *J.*, 1951, 881.
[10] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 67.
[11] Marvel and Hiess, *Org. Synth.*, Coll. Vol. I, 1944, 327.
[12] I. G. Farbenind., B.P., 308,740; *Chem. Zentr.*, 1930, II, 2185.
[13] Cf. Mitchell and Trautner, *J.*, 1947, 1330.
[14] Butenandt, Biekert, and Neubert, *Angew. Chem.*, 1956, **68**, 379.

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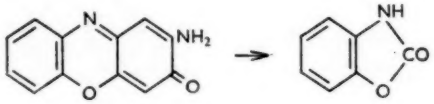
actinomycin with alkaline hydrogen peroxide is a peptide, possibly attached to a small molecule. Its investigation is still in progress but it is obvious from the yields that the two peptide-containing products cannot be derived from the same peptide chain in the actinomycin molecule. This oxidative fission of actinomycin therefore provides a method for distinguishing the two peptide groups and hence should prove to be of value in elucidating



(VI)

the precise structure of the various members of the actinomycin group. The techniques used by Brockmann and his colleagues for elucidation of the order of the amino-acids in the peptides were applied to the whole molecule, and such methods are much less valuable when the peptide chains are not identical.

Experimental

95% Ethanol was used as the solvent in determinations of ultraviolet absorption spectra except where otherwise stated.

Oxidation of Actinomycin B with Alkaline Hydrogen Peroxide.—Actinomycin B (recrystallised; 1·01 g.) was dissolved in the minimum amount (*ca.* 80 c.c.) of methanol, and an excess of alkaline hydrogen peroxide (100 c.c. of a 3% solution in 0·75N-sodium hydroxide) was added with stirring. After 1 hr. at room temperature the pH was adjusted to 3—4 by dilute hydrochloric acid, and the solution was diluted with water (250 c.c.). The product was extracted with butan-1-ol (3 × 100 c.c.), the combined butanol extracts were washed, and the solvent was removed under reduced pressure, to leave a pale yellow solid resin (0·86 g.). Examination of this product by chromatography on Whatman No. 1 paper, with propan-2-ol–aqueous ammonia (*d* 0·88)–water (7 : 1 : 2) as solvent, revealed the presence of four spots fluorescent in ultraviolet light, R_F 1·0 (*a*), 0·75 (*b*), 0·45 (*c*), and 0·40 (*d*) respectively. Of these, spot (*b*) was intensely fluorescent and the others were only faintly fluorescent; material (*a*) was non-acidic and the other three were acidic. A rough separation of the mixture was achieved by dissolving the crude product in acetone–ethyl acetate (1 : 9; 70 c.c.), separating any undissolved solid, and extracting the solution with saturated sodium hydrogen carbonate solution (3 × 40 c.c.). The aqueous layer was then acidified with hydrochloric acid and extracted with chloroform (3 × 50 c.c.) and then with butan-1-ol (2 × 50 c.c.). Examination of the various solutions by paper chromatography as before showed that the residual yellow ethyl acetate solution contained substance (*a*) of R_F 1·0, and evaporation of the solution gave it as a bright yellow solid (125 mg.) which was not examined further. The mixed chloroform extracts contained most of substance (*b*) of R_F 0·75 and evaporation gave a pale yellow solid (260 mg.). The butan-1-ol extracts contained substances (*c*) and (*d*), of R_F 0·45 and 0·40 respectively, and a little of substance (*b*). Evaporation of the solvent gave a pale yellow solid (304 mg.) which showed only very weak absorption at 250 mμ and was therefore largely composed of peptides. The examination of this product will be described in a later paper.

Fraction (*b*) was purified by counter-current extraction between ethyl acetate and 0·1M-phosphate buffer (pH 5·9). The solution was subjected to 24 transfers and the distribution of the product followed by measurement of the intensity of light absorption at 300 mμ; it was found that most of substance (*b*) was located in tubes 2—13. The contents of these tubes were mixed and acidified and the organic layer was separated and washed. After removal of the solvent, the *product* was obtained as a pale buff solid (90 mg.) which crystallised from ethyl acetate–light petroleum (b. p. 60—80°) as very small prisms, m. p. 233° (Found: C, 53·9; H, 7·2; N, 11·3. $C_{32}H_{44}O_{10}N_6,2H_2O$ requires C, 54·2; H, 6·8; N, 11·85%). The product was acidic, having pK_a 3·7 in glycol monomethyl ether–water (1 : 9), equiv. (titration), 632 ($C_{32}H_{44}O_{10}N_6$ requires 673), and light-absorption max. at 246 and 296—297 mμ (log ε 4·05 and

3·63 respectively). The principal bands in the infrared spectrum (Nujol mull) were at 3300, 1786, 1740, and 1666—1625 (broad) cm.$^{-1}$. The product gave a brownish-red ferric reaction.

Acid Hydrolysis of the Hydrogen Peroxide Oxidation Product of Actinomycin.—The crude oxidation product (1 g.) was dissolved in 6N-hydrochloric acid (25 c.c.) and heated overnight at 80° under oxygen-free nitrogen. The brown solution was cooled, adjusted to pH 4 by sodium hydrogen carbonate, and extracted with butan-1-ol (3 × 50 c.c.). The butanol extract was washed and the solvent removed under reduced pressure, to leave a brown gum (80—100 mg.), which was sublimed at 140°/0·5 mm., to give a sticky yellow solid (40—60 mg.). This was crystallised from water, and the pale yellow solid so obtained further purified by sublimation as before. The colourless solid (5 mg.) had no definite m. p. but darkened above 235°. After recrystallisation from methanol *7-methylbenzoxazolone-4-carboxylic acid* formed needles [Found: C, 56·5; H, 4·0, 3·9; N, 7·9, 7·3%; *M* (isopiestic method),[15] 187 ± 7. $C_9H_7O_4N$ requires C, 56·0; H, 3·6; N, 7·3%; *M*, 193]. Light absorption: (i) max. at 300—303, 244—245, and 212—213 mμ (log ε 3·68, 4·02, and 4·48 respectively), unchanged on acidification with dilute hydrochloric acid; (ii) in 95% ethanol–0·1N-aqueous sodium hydroxide (1 : 1): max. at 303—304, 250, and 218—219 mμ (log ε 3·72, 4·03, and 4·32 respectively). The infrared spectrum (KBr) showed bands at 3175, 3077, 2915, 2740—2500 (diffuse), 1764 (s), 1695, 1653, 1623, 1605, 1508, 1422 (s), 1389, 1333 (s), 1290, 1258 (s), 1205, 1171, 1145, 1117, 1087, 1038, 1003, 971, 961, 833, 810, 775 (s), 758 (s), 739 (s), and 680 cm.$^{-1}$. A similar determination on a chloroform solution showed bands at 1799 (s), 1695, and 1647 cm.$^{-1}$ in the carbonyl region.

The product was acidic and could be extracted from aqueous solutions of pH <5 into organic solvents, *e.g.*, ether, ethyl acetate, and butan-1-ol. It coupled with diazotised sulphanilic acid to give a red product but could not be diazotised itself. Tests for a primary amide group were negative and the compound gave no ferric reaction. With Ehrlich's reagent it gave a yellow colour similar to that obtained from 3-hydroxyanthranilic acid.

Oxidation of 2-Aminophenoxazin-3-one.—2-Aminophenoxazin-3-one[16] (100 mg.) was dissolved in methanol (10 c.c.) and treated with an alkaline solution of hydrogen peroxide (1·5 c.c. of 30%; 3 c.c. of 10% aqueous sodium hydroxide; and 10 c.c. of water). No visible reaction occurred after 30 min. at room temperature but at 50° the solution was rapidly decolorised. After cooling and acidification, the mixture was extracted with chloroform (3 × 20 c.c.) and the combined extracts, which showed a strong green fluorescence in ultraviolet light, were washed, dried, and evaporated. The dark brown resinous product (15 mg.) was sublimed at 140°/0·1 mm. and gave two products. The less volatile (2 mg.) had m. p. 140° alone and mixed with sublimed benzoxazolone.

2-Methoxy-m-toluidine Hydrochloride.—Raney nickel (10 g. as sludge in ethanol) was added to a solution of 2-methoxy-3-nitrotoluene[17] (35 g.) in dry ethanol (50 c.c.) and hydrogenated in an autoclave at room temperature and 4 atm. of hydrogen. The reduction was complete in 20 min., then the catalyst was removed and the filtrate diluted with ether (150 c.c.). The solution was saturated with hydrogen chloride, and the precipitated hydrochloride of 2-methoxy-*m*-toluidine (35 g.) was separated and washed with ether. It had m. p. 112° (sealed capillary) after crystallisation from methanol–ether.

7-Methoxy-6-methylisatin.—A solution of 2-methoxy-*m*-toluidine hydrochloride (10 g.) in 3N-hydrochloric acid (50 c.c.) was added to an aqueous solution (120 c.c.) of chloral hydrate (9 g.) and anhydrous sodium sulphate (130 g.). A solution of hydroxylamine hydrochloride (11 g.) in water was then added and the whole brought to 90° during 1 hr., then boiled for 10 min., cooled, and kept overnight. Crystalline hydroxyiminoacetyl-2-methoxy-*m*-toluidine (9 g.; air-dried) separated in a form pure enough for the subsequent cyclisation.

The hydroxyimino-compound was added gradually with stirring to concentrated sulphuric acid (56 g.; *d* 1·8), at 55° on the steam-bath. The temperature of the mixture rose rapidly to 80—90° and, after the addition of all of the solid, the mixture was kept at this temperature for a further 20 min. The cooled dark red solution was poured on ice (300 g.) and kept for 2 hr., then the deep red aqueous suspension was extracted with ether (5 × 50 c.c.). Removal of the solvent from the combined washed and dried ethereal extract yielded an orange solid (3 g.) which was crystallised from a small volume of chloroform and sublimed at 140°/0·5 mm., to give *7-methoxy-6-methylisatin* as orange-red needles, m. p. 169° (Found: C, 62·8; H, 4·8; N, 7·55.

[15] Morton, Campbell, and Ma, *Analyst*, 1953, **78**, 722.
[16] Zincke and Hebebrand, *Annalen*, 1884, **226**, 60.
[17] Robinson, *J.*, 1916, **109**, 1084.

$C_{10}H_9O_3N$ requires C, 62·8; H, 4·75; N, 7·3%). Light absorption: (i) max. at 420—424, 317—319, 246, and 224 mμ (log ε 2·97, 3·76, 4·22, and 3·97 respectively); (ii) in 95% ethanol–0·1N-aqueous sodium hydroxide (1 : 1): max. at 370, 272—273, and 231 mμ (log ε 3·68, 4·05, and 4·34 respectively). Infrared spectrum (Nujol mull): max. at 3140, 2945, 1740, 1620, 1593, 1490, 1430, 1370, 1317, 1280, 1240, 1195, 1150, 1062, 1013, 957, 875, 828, 787, 772, and 730 $cm.^{-1}$.

Contrary to the recommended procedure for the cyclisation of hydroxyiminoacetanilide [11] which was dried before addition to the sulphuric acid, it was found in this case that the cyclisation was more rapid if slightly damp samples of our 2-methoxy-compound were used. In one experiment with material which had been dried in a vacuum-desiccator, no isatin was obtained after the treatment with hot sulphuric acid.

7-Hydroxy-6-methylisatin.—7-Methoxy-6-methylisatin (0·89 g.) was mixed with freshly prepared pyridine hydrochloride (2·5 g.) and heated at 210° (oil-bath) for 1 hr.[18] The melt was cooled, then treated with water (25 c.c.), and the dark red insoluble material separated. The filtrate was extracted with ether, and the extract washed, dried, and evaporated. The residue was combined with the water-insoluble material and dissolved as far as possible in boiling ethanol (150 c.c.). After clarification with charcoal, most of the solvent was removed and water added until solid began to separate. This redissolved when the solution was heated and, after cooling, dark brownish-red needles (0·6 g.) were obtained which decomposed at 220° without melting. The *product* sublimed at 180°/0·5 mm. as long dark red needles (Found: C, 61·4; H, 4·1; N, 8·1. $C_9H_7O_3N$ requires C, 61·0; H, 4·0; N, 7·9%). Light absorption: (i) max. at 448—452, 430—446 (broad), 335—337, and 224—225 mμ (log ε 3·04, 3·04, 3·79, and 4·29 respectively); (ii) in 95% ethanol–0·1N-aqueous sodium hydroxide (1 : 1): max. at 406, 301, and 255 mμ (log ε 3·49, 4·09, and 4·28 respectively).

7-Methylbenzoxazolone-4-carboxylic Acid.—7-Hydroxy-6-methylisatin (0·15 g.) was dissolved in methanol (4 c.c.) and a solution of 30% hydrogen peroxide (1·5 c.c.) in aqueous 2·5% sodium hydroxide (13·5 c.c.) was added. The mixture was kept for 5 min. at room temperature, then acidified with 2N-hydrochloric acid to pH 2 and extracted with butan-1-ol (2 × 25 c.c.). The extract was washed and dried and the solvent removed, to leave a brownish solid which was purified by sublimation at 160°/0·1 mm. The main product (0·1 g.) was a colourless solid which was crystallised from hot water and resublimed. A minor product was not investigated further. The principal oxidation product, *7-methylbenzoxazolone-4-carboxylic acid*, decomposed without melting at 240° (Found: C, 55·7; H, 3·9; N, 7·5. $C_9H_7O_4N$ requires C, 56·0; H, 3·65; N, 7·25%). It gave no ferric reaction and on chromatography on paper with propan-2-ol–aqueous ammonia (*d* 0·88)–water (7 : 1 : 2) it had R_F 0·6. The ultraviolet and infrared spectra were identical with those obtained for the product from actinomycin (see above).

6-Methoxy-m-toluidine.—Raney nickel (5 g. as sludge in ethanol) was added to a solution of 4-methoxy-3-nitrotoluene in ethanol (40 c.c.) and the mixture hydrogenated in an autoclave at room temperature and 4 atm. hydrogen. Reduction was complete in 4 hr., then the catalyst and solvent were removed. The residue (13·5 g.) formed colourless crystals, m. p. 45°, which, without purification, were used in the following experiment.

7-Methoxy-4-methylisatin.—A solution of 6-methoxy-*m*-toluidine (4·5 g.) in 3N-hydrochloric acid (25 c.c.) was added to an aqueous solution (60 c.c.) of chloral hydrate (4·5 g.) and anhydrous sodium sulphate (65 g.). A solution of hydroxylamine hydrochloride (6·5 g.) in water (25 c.c.) was added and the whole brought slowly to 90° (1 hr.) and then boiled for 10 min. After cooling, the colourless crystals (4 g.) of hydroxyiminoacetyl-6-methoxy-*m*-toluidine were separated and air-dried. This product (2 g.) was added gradually with stirring to sulphuric acid (15 g.; *d* 1·8) at 50°. The temperature of the mixture rose rapidly to 90—100° and, after the addition of all of the solid, was kept thereat for a further 20 min. The cooled dark red solution was poured on ice (100 g.), and the red precipitate separated. A further quantity was deposited from the filtrate on storage. The combined solid product (1·1 g.) was crystallised from ethyl acetate, forming dark red crystals, m. p. 234° (lit.,[12] 235—236°), which sublimed at 140°/0·5 mm. (Found: C, 63·05; H, 4·5; N, 7·65. Calc. for $C_{10}H_9O_3N$: C, 62·8; H, 4·75; N, 7·3%). Light absorption: max. at 459, 327—332, and 227—229 mμ (log ε 3·17, 3·53, and 4·27 respectively).

7-Hydroxy-4-methylisatin.—7-Methoxy-4-methylisatin (100 mg.) was heated with freshly prepared pyridine hydrochloride (200 mg.) at 200° (oil-bath) for 5 min. The melt was cooled and treated with water (5 c.c.), and the red insoluble material separated, washed, and dried. Fractional vacuum-sublimation at 140°/0·5 mm. gave the unchanged methoxy-compound but

[18] Cf. Prey, *Ber.*, 1941, **74**, 1219.

at 190°/0·5 mm. the hydroxy-compound was obtained as dark red needles (10 mg.). The sublimed *product*, when crystallised from aqueous ethanol and resublimed, had m. p. 269° (Found: C, 61·3; H, 4·0; N, 8·15. $C_9H_7O_3N$ requires C, 61·0; H, 4·0; N, 7·9%). Light absorption: max. at 464—469, 335—336, and 227 mμ (log ε 3·22, 3·61, and 4·26 respectively).

5-Methylbenzoxazolone-4-carboxylic Acid.—7-Hydroxy-4-methylisatin (50 mg.) was dissolved in methanol (2 c.c.) and a solution of 30% hydrogen peroxide (0·5 c.c.) in aqueous 2·5% sodium hydroxide (5·5 c.c.) was added. The mixture was kept at room temperature for 5 min., then acidified with dilute hydrochloric acid and extracted with butan-1-ol (2 × 10 c.c.). The butanol extract was washed and the solvent removed, leaving a pale brown solid (35 mg.) which was purified by sublimation at 185°/0·5 mm. The colourless *acid* crystallised from very dilute ethanol and was then resublimed (Found: C, 56·1; H, 3·9; N, 7·5. $C_9H_7O_4N$ requires C, 56·0; H, 3·65, N, 7·25%). The infrared spectrum (Nujol mull) showed bands at 3226, 1908, 1779 (s), 1745 (s), 1709 (s), 1626, 1610, 1312, 1292, 1258 (s), 1136, 1124, 1040, 1026, 962, 943, 855, 826, 809, 800, 793, 786, 752, and 727 cm.$^{-1}$.

We are greatly indebted to Dr. D. W. Henderson and Mr. R. Elsworth of the Ministry of Supply Microbiological Research Station, Porton, and their colleagues, for the production of substantial amounts of actinomycin B concentrate. We also acknowledge a gift of actinomycin B from Dr. J. A. Aeschlimann of Hoffmann–La Roche Inc., Nutley, New Jersey. One of us (E. B.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

Department of Chemistry, The University, Nottingham. [*Received, September 13th*, 1956.]

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308. *Chemistry of the Higher Fungi. Part VIII.* A Series of Acetylenic Compounds from* Polyporus anthracophilus.

By J. D. Bu'Lock, E. R. H. Jones, and W. B. Turner.

The separation and characterisation of a series of acetylenic derivatives of *n*-decane and *n*-octane, metabolic products of the Basidiomycete *P. anthracophilus*, are described. The compounds are shown to be ethylenic-acetylenic alcohols, acids, hydroxy-acids and diacids, with oxygen functions at one or both ends of the molecule; the acids occur free, as methyl esters, and as esters with the hydroxy-compounds of the series.

With the exception of an acetylenic thiophen derivative, junipal, which was detected as an odoriferous metabolite of *Daedalea juniperina*,[1] the fungal polyacetylenes so far described in the literature are all produced by organisms which first attracted interest because of their antibiotic-producing activity. For comparative purposes, and with a view to biochemical studies, we wished to add further examples to the list of natural acetylenes, and a more selective approach seemed desirable. The need was in part met by our observation that some polyacetylene derivatives could be detected spectroscopically in crude extracts from malt-agar slope cultures of certain fungi. Several hundred species of wood-rotting Basidiomycetes (supplied through the kindness of the Director of the Forest Products Research Laboratory, Princes Risborough) were examined in this way and a number selected for further study; some of the results obtained with one of these are reported here.

The fungus is an Australian species, *Polyporus anthracophilus*, which grows well on the semi-synthetic medium used earlier.[2]

The yield of acetylenic compounds is very variable, but in general up to about 1% of the carbon supplied to the cultures as glucose has been accounted for as acetylenic compounds. For comparison it may be observed that our cultures appeared to convert

* Part VII, *J.*, 1957, 1097.

[1] Birkinshaw and Chaplen, *Biochem. J.*, 1955, **60**, 255.

[2] Bu'Lock and Leadbeater, *ibid.*, 1956, **62**, 476.

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about 0·5% of the carbon supplied as glucose into triterpenoids of the eburicoic acid type,[3] whilst with another Basidiomycete yields of polyacetylene derivatives of over 3% (based on carbon *utilised* from glucose) have been obtained.[2] The acetylenic metabolites of *P. anthracophilus* constitute a complex and variable mixture of at least seventeen compounds; these are closely related and so form an interesting series. The thirteen metabolites which we have characterised fully are represented by formulæ (I)—(VIII). The acids of this series occur free, and also combined as methyl esters and the more complex esters (VII) and (VIII). Some other components of the mixture are discussed on p. 1611.

(I) $CH_3{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2R$ $CH_3{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CH_2{\cdot}OH$ (II)

(III) $HO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2R$ $RO_2C{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2R$ (IV)

(V) $RO_2C{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2R$ $RO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2R$ (VI)

$CH_3{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2{\cdot}CH_2{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CH_3$ (VII)

$CH_3{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2Me$ (VIII)

(R = H or Me; all ethylenic bonds *trans*.)

The extraction of *P. anthracophilus* cultures and fractionation of the extracts are described in the Experimental section. It should be noted that the composition of extracts from the cultures was very variable, depending in rather a complex way upon the duration of fermentation. The general procedure in working-up was to separate neutral and acidic fractions and to methylate the latter. Fractions were then further resolved by repeated chromatography on alumina. The order of elution from the columns was a useful guide to the constitution of particular fractions, since the compounds always appeared in order of increasing polarity, *i.e.*, esters < diesters < alcohols < hydroxy-esters.

The ester (I; R = Me) is the most important acetylene derivative produced by *P. anthracophilus*; it is present mainly in the mycelium but occurs to the limit of its solubility in the aqueous medium. The free acid (I; R = H) occurs in comparatively small amounts. The ester crystallises readily; it was shown to contain the $\cdot CH{=}CH{\cdot}[C{\equiv}C]_2{\cdot}CH{=}CH{\cdot}CO_2R$ chromophore by its ultraviolet absorption spectrum and to be a derivative of methyl decanoate by hydrogenation and conversion of the product into methyl 3 : 5-dinitrobenzoate and decananilide. The infrared spectrum of the ester shows peaks at 945 and 955 cm.$^{-1}$ (*trans*-CH=CH–) and 1720 cm.$^{-1}$ (αβ-unsaturated ester). All these data identify it as methyl deca-*trans*-2 : *trans*-8-diene-4 : 6-diynoate (I; R = Me), *i.e.*, the *trans* : *trans*-matricaria ester synthesised by Sörensen *et al.*[4] The ultraviolet absorption spectra of (I; R = Me) (Fig. 1) and of its *cis*-2 : *trans*-8- and *cis*-2 : *cis*-8-isomer [4] are anomalous in that in them the characteristic acetylenic fine-structure spacing (*ca.* 2200 cm.$^{-1}$) is not sharp. The symmetrical diester (IV; R = Me) shows almost the same absorption maxima as the ester (I; R = Me) but with typical sharp fine-structure (Fig. 1); reasons for this are obscure.

Unlike the above ester (I; R = Me), the corresponding alcohol (II) is found mainly in the aqueous medium, and is the principal acetylenic constituent in rather old (150-day) cultures. It has the ultraviolet absorption spectrum of the $\cdot CH{=}CH{\cdot}[C{\equiv}C]_2{\cdot}CH{=}CH\cdot$ chromophore and its infrared spectrum indicates the presence of *trans*-CH=CH· and a hydroxyl group. Hydrogenation gave decanol (3 : 5-dinitrobenzoate), and identification of the alcohol as deca-*trans*-2 : *trans*-8-diene-4 : 6-diyn-1-ol (II) was confirmed by direct comparison with a synthetic [4] specimen of *trans* : *trans*-matricarianol kindly supplied by Professor Sörensen, and also with material obtained by reduction of the ester (I; R = Me) with lithium aluminium hydride at −50°.

The hydroxy-ester (III; R = Me) also accumulates preferentially in the aqueous medium, together with the corresponding acid. Hydrolysis of the low-melting ester

[3] Gascoigne, Holker, Ralph, and Robertson, *J.*, 1951, 2346.
[4] Bruun, Christensen, Haug, Stene, and Sörensen, *Acta Chem. Scand.*, 1951, **5**, 1244.

gave the crystalline acid. Both show the ultraviolet absorption spectrum of the diyne-ene-carbonyloxy-chromophore; comparison of the infrared spectra of the ester and of synthetic [5] methyl dec-*trans*-2-ene-4 : 6-diynoate (*trans*-lachnophyllum ester) showed many similarities but that of the natural ester contained extra bands attributable to a primary hydroxyl group. Hydrogenation of the acid, followed by chromic acid oxidation, gave sebacic acid, which suggested the structure methyl 10-hydroxydec-*trans*-2-ene-4 : 6-diynoate (III; R = Me) for the natural ester. This was therefore synthesised by the oxidative coupling of pent-4-yn-1-ol and methyl pent-*trans*-2-en-4-ynoate. The low-melting product was spectroscopically identical with the natural ester and on hydrolysis gave the acid (III; R = H).

From the mixture of acids produced by *P. anthracophilus* the diacid (IV; R = H) could be isolated by virtue of its relative insolubility in organic solvents; both the free acid and its dimethyl ester occur in the cultures. As already noted, both show ultraviolet absorption with maxima quite close to those of matricaria esters but differing in having sharp fine-structure (Fig. 1). The chromophore could not be immediately identified but clearly it involved at least nine carbon atoms, and since the equivalent weight of the acid was *ca.* 100 it was presumed to be dibasic. Hydrogenation gave sebacic acid, so that the natural acid is deca-*trans*-2 : *trans*-8-diene-4 : 6-diyne-1 : 10-dioic acid (IV; R = H), which had been previously synthesised together with the dimethyl ester by Heilbron *et al.*[6] Repetition of the synthesis confirmed this identification.

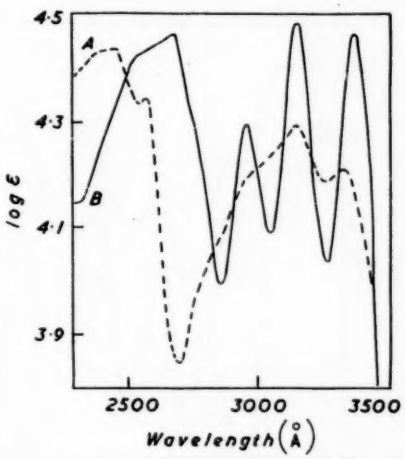

FIG. 1. *Ultraviolet absorption spectra (in ethanol) of* (I; R = Me) (*curve* A) *and* (IV; R = Me) (*curve* B) *showing fine-structure differences.*

The acids from *P. anthracophilus* having been converted into the methyl esters, the separation of another dimethyl ester $C_6H_4(CO_2Me)_2$ (V; R = Me) from the above diester (IV; R = Me) was only achieved with some difficulty. The ultraviolet absorption spectrum of this compound shows no acetylenic fine-structure, but instead resembles that of a polyene ester. Its infrared absorption spectrum shows only one carbonyloxy-peak (αβ-unsaturated), and the acetylenic band (*ca.* 2200 cm.$^{-1}$) is absent. However, the intensity of the ultraviolet absorption is much lower than would be expected for a diethyl octa-2 : 4 : 6-triene-1 : 8-dioate and comparable to that recorded [7] for dimethyl octa-2 : 4-dien-6-yne-1 : 8-dioate; such a lowering of the extinction coefficient is the characteristic effect of replacing a double by a triple bond. The infrared spectrum of the diester differs from that of dimethyl octa-2 : 4-dien-6-yne-1 : 8-dioate since the latter shows a strong band at 2200 cm.$^{-1}$ due to the triple bond,[7] but its properties are consistent with the structure dimethyl octa-*trans*-2 : *trans*-6-dien-4-yne-1 : 8-dioate (V; R = Me) (in this the triple bond is symmetrically placed so that its stretching vibration is inactive in infrared absorption). Accordingly, we found that the diester would not react with maleic anhydride despite the *trans*-configuration of its double bonds (deduced from the infrared spectrum); this observation renders structures with adjacent double bonds unlikely.

[5] Sample prepared by Mr. Ian Bell; cf. Bruun, Haug, and Sörensen, *Acta Chem. Scand.*, 1950, **4**, 850.

[6] Heilbron, Jones, and Sondheimer, *J.*, 1947, 1586.

[7] Jones, Shaw, and Whiting, *J.*, 1954, 3212.

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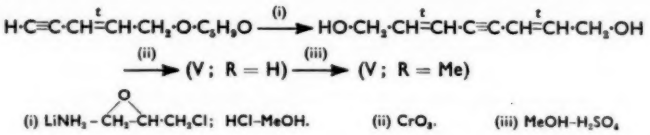
Neither the acid (V; R = H) nor its ester (V; R = Me) had been described previously, and therefore the ester was synthesised from *trans*-pent-2-en-4-yn-1-yl tetrahydropyranyl ether by the route outlined below. The product was identical with the naturally-derived compound.



A third diacid (VI; R = H) shows an ultraviolet absorption spectrum of the diyn-ene-carbonyloxy-type already encountered in the hydroxy-ester (III). However, comparison of the infra-red spectra showed that the corresponding ester contains no hydroxyl group;

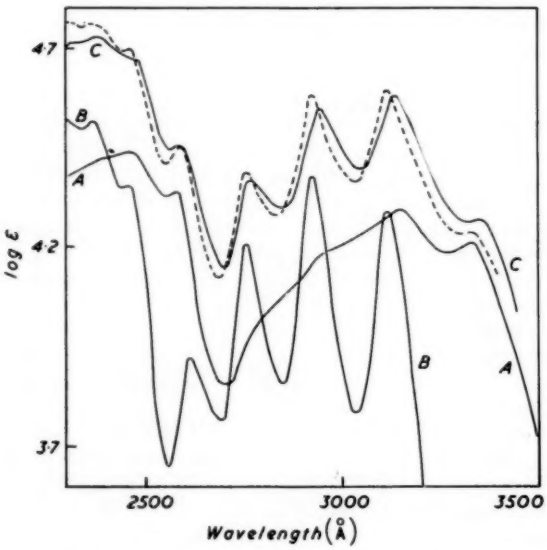


FIG. 2. *Ultraviolet absorption spectra (in ethanol) of* (I; R = Me) (*curve* A), (II) (*curve* B), *and* (VII) (*curve* C). *The broken line indicates the summation of curves* A *and* B.

on the other hand it contains two dissimilar ester groups, revealed by bands at 1740 cm.$^{-1}$ and 1720 cm.$^{-1}$ ($\alpha\beta$-unsaturated). Formulation of this diester as dimethyl dec-*trans*-2-ene-4 : 6-diyne-1 : 10-dioate (VI; R = Me) was confirmed by synthesis of this compound by chromic acid oxidation of the hydroxy-ester (III; R = Me) and methylation of the product.

The nature of the "mixed esters" (VII) and (VIII) was first deduced from their absorption spectra. The ester (VII) gave an ultraviolet spectrum almost identical with that obtained by summation of the curves for the methyl ester (I; R = Me) and the alcohol (II) (cf. Fig. 2), whilst in its infrared spectrum the intensity of the carbonyl band was approximately one-half of that in the spectrum of (I; R = Me). Similarly, the ultraviolet absorption spectrum of the diester (VIII) could be duplicated by summation of the curves for the ester (I; R = Me) and the hydroxy-ester (III; R = Me) (Fig. 3). Both structures were fully confirmed by the synthesis of (VII) and (VIII) from the chloride of the acid (I; R = H) and the hydroxy-compounds (II) and (III; R = Me), respectively. Having regard to the circumstances of their isolation, we consider the esters (VII) and (VIII) to be genuine metabolites of *P. anthracophilus* and not artefacts formed during the working-up process.

With the exception of the C_8-diester (V; R = Me) and of the " mixed esters " (VII) and (VIII) the formulæ of the compounds so far described can be summarised in (IX). Of the fifteen possibilities represented by this general formula (IX) we have described the characterisation of five compounds, *viz.*, (I), (II), (III), (IV), and (VI). Of the remaining possibilities, two are hydrocarbons and two are glycols, and we have had no indication of the production of either class of compound by *P. anthracophilus*. Some of the possi-

$$\left.\begin{matrix}CH_3\\CH_2\cdot OH\\CO_2H\end{matrix}\right\}\left\{\begin{matrix}\cdot CH{=}CH\cdot[C{\equiv}C]_2\cdot CH{=}CH\cdot\\\cdot CH_2\cdot CH_2\cdot[C{\equiv}C]_2\cdot CH{=}CH\cdot\end{matrix}\right\}\left\{\begin{matrix}CH_3\\CH_2\cdot OH\\CO_2H\end{matrix}\right. \quad \text{(IX)}$$

(All ethylenic bonds *trans*.)

bilities, if produced only in trace amounts, might well have escaped detection, but there are indications that at least four further members of the series are produced by the fungus.

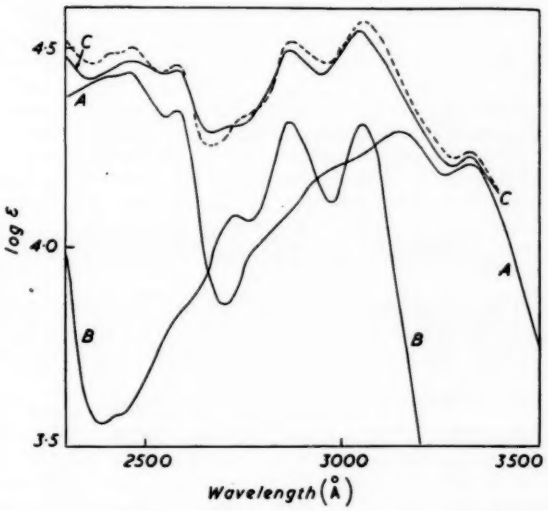


FIG. 3. *Ultraviolet absorption spectra (in ethanol) of* (I; R = Me) (*curve* A), (III; R = Me) (*curve* B), *and* (VIII) (*curve* C). *The broken line indicates the summation of curves* A *and* B.

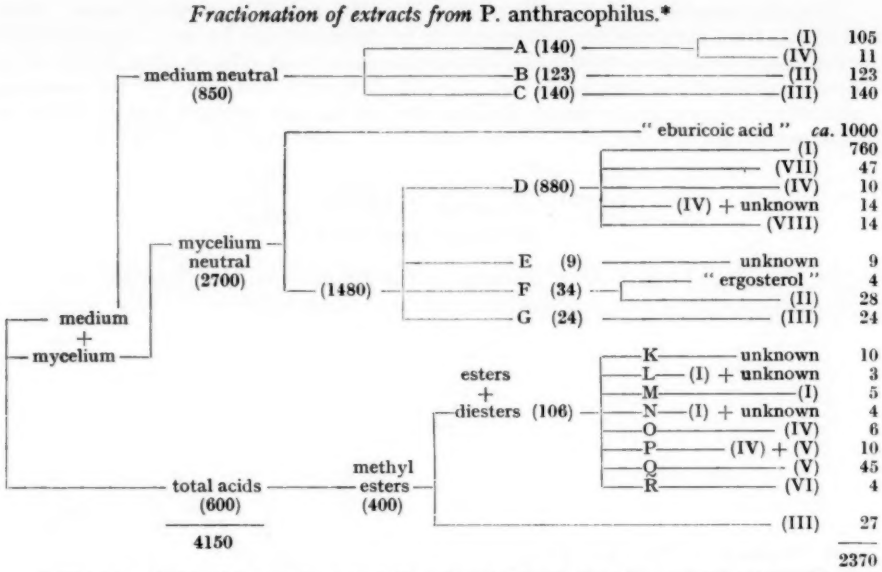
A neutral compound which behaves on alumina as an alcohol, and having the absorption spectrum of an ene-diyne, might well be one of the two possible decenediynols represented by the above formula. Similarly a compound with a characteristic ultraviolet absorption

$$HO\cdot CH_2\cdot CH{=}CH\cdot C{\equiv}C\cdot C{\equiv}C\cdot CH{=}CH\cdot CO_2Me \quad \text{(X)}$$

spectrum, similar to that of (I; R = Me), but which behaves on alumina as a hydroxy-ester, is probably the hydroxy-ester (X). A third compound, possibly the methyl ester of the conjugated decenediynoic acid, has the ultraviolet absorption spectrum of the hydroxy-ester (III; R = Me) but behaves on alumina like the non-hydroxylic ester (I; R = Me), whilst a fourth is of similar polarity but has the ultraviolet absorption of an ene-diyne, and thus might be an ester of the isomeric decenediynoic acid with the carbonyloxy-group not in conjugation. These compounds occur in minute amounts, but may occur in larger quantities in other strains of *P. anthracophilus* or in some apparently related species now being studied. In addition to these acetylenic compounds, our *P. anthracophilus* cultures contained an appreciable quantity of, presumably, eburicoic and dehydroeburicoic acid [3] and smaller amounts of ergosterol-like material (cf. Experimental).

The acetylenic compounds from *P. anthracophilus* may be compared with the series of C_{10} polyacetylene derivatives from Compositae extensively studied by the Sörensens

Fractionation of extracts from P. anthracophilus.*



* Weights noted in this flow-sheet, including those in the final column, are the total weights (in mg.) of fractions after evaporation. Yields of recrystallised material are given in the text.

and their co-workers.[8] Indeed our isolation of the alcohol (II) (*trans* : *trans*-matricarianol) provides the first example of the occurrence of the same polyacetylene in fungi and in higher plants.[9] However, despite common features there are three important differences between

Ultraviolet absorption spectra in ethanol: $\lambda_{max.}$ (Å) *and* log ε (*in parentheses*).

I; R = Me †	—	—	—	2340 * (4·38)	2460 (4·41)	2580 (4·32)	2960 * (4·20)	3140 (4·28)	3330 (4·20)	—
I; R = H †	—	—	—	—	2450 (4·37)	2560 (4·27)	—	3100 (4·23)	3290 (4·16)	—
II	—	2175 (4·51)	2315 (4·53)	2370 (4·52)	2470 (4·35)	2610 (3·94)	2760 (4·23)	2930 (4·39)	3120 (4·30)	—
III; R = Me	—	2150 (4·45)	2230 (4·53)	—	2430 * (3·58)	2580 * (3·83)	2730 (4·08)	2870 (4·31)	3050 (4·30)	—
III; R = H	—	2150 (4·48)	2220 (4·56)	—	2430 * (3·66)	2550 * (3·81)	2700 (4·10)	2850 (4·32)	3030 (4·31)	—
IV; R = Me	—	2160 (4·39)	—	—	—	—	2690 (4·45)	2980 (4·29)	3170 (4·48)	3390 (4·46)
IV; R = H	—	2160 (4·38)	—	—	—	2580 * (4·41)	2670 (4·26)	2960 (4·26)	3150 (4·44)	3380 (4·42)
V; R = Me	2050 * (4·04)	2140 (4·06)	—	—	2400 * (4·00)	—	2780 * (4·27)	2920 (4·44)	3070 (4·40)	—
VI; R = Me	—	2145 (4·42)	2230 (4·54)	—	2430 * (3·28)	2550 * (3·69)	2700 (4·08)	2850 (4·32)	3030 (4·31)	—
VII		2130 (4·66)	2330 * (4·71)	2385 (4·72)	2460 * (4·68)	2590 (4·45)	2775 (4·36)	2950 (4·55)	3140 (4·58)	3350 (4·28)
VIII	—	—	2230 (4·72)	—	2465 (4·45)	2590 (4·42)	—	2870 (4·52)	3050 (4·57)	3340 (4·22)

* Inflexion. † Compare Sörensen *et al.*[4]

the two series. First, all the compounds from *P. anthracophilus* are *trans*- or *trans* : *trans*-isomers; this contrasts sharply with the Compositae series where the *cis*-configuration is more common. Secondly, the occurrence in *P. anthracophilus* of the eight-carbon

[8] Sörensen, *Chem. and Ind.*, 1953, 240.
[9] Holme and Sörensen, *Acta Chem. Scand.*, 1954, **8**, 34.

system (V) is not paralleled in the Compositae though this chain length is known in other fungal acetylenes, *e.g.*, junipal,[1] diatretyne I, and agrocybin.[10] Thirdly, the compounds with oxygen functions at both ends of the carbon chain are without parallel in the Compositae, though such structures are typical of certain other fungal acetylenes.[10]. The biogenetic implications of these and other observations with *P. anthracophilus* are to be discussed more fully elsewhere.

Experimental

Ultraviolet absorption spectra, cf. Table, were measured in ethanol (chromatographic fractions were examined directly) on Unicam SP-500 instruments, infrared absorption spectra on a Perkin-Elmer Model 21 spectrophotometer, and m.p.s (corrected) on a Kofler block. Alumina for chromatography was Peter Spence grade " H," deactivated by treatment with 5% of 10% acetic acid. Light petroleum refers to the fraction with b. p. 60—80°. Evaporations were carried out under reduced pressure in nitrogen.

Characterisation and Synthesis of the Components.

Methyl Deca-trans-2 : trans-8-*diene*-4 : 6-*diynoate* (trans : trans-*Matricaria Ester*) (I; R = Me).—This ester crystallised from aqueous ethanol or light petroleum as needles, m. p. 62—63° (lit., m. p. 60—61°) (Found : C, 75·3; H, 5·6. Calc. for $C_{11}H_{10}O_2$: C, 75·8; H, 5·8%), with an ultraviolet absorption spectrum (cf. Table) agreeing closely with that described by Sörensen *et al.*[4] The compound (300 mg.), hydrogenated in light petroleum over 2% palladium on calcium carbonate (500 mg.), gave methyl decanoate, which was converted directly into methyl 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 106·5—109·5°, and decananilide, m. p. and mixed m. p. 63—65°. Reaction of the ester (I; R = Me) (100 mg.) in methanol (8 c.c.) with aqueous potassium hydroxide (200 mg. in 9 c.c.; 8 hr. at 0° under nitrogen) and isolation of the acidic product gave, after recrystallisation from acetone–light petroleum, deca-*trans*-2 : *trans*-8-diene-4 : 6-diynoic acid (*trans* : *trans*-matricaria acid) (I; R = H), plates, m. p. 175—177° (decomp.) [lit., m. p. 173° (decomp.)] with an ultraviolet absorption spectrum (cf. Table) in agreement with the data of Sörensen *et al.*[4] Reduction of the ester (I; R = Me) (19 mg.) in dry ether (25 c.c.), cooled in solid carbon dioxide–acetone, with a solution of lithium aluminium hydride in ether (*ca.* 50% excess), washing the solution with dilute sulphuric acid and water, evaporation of the solvent, and crystallisation of the residue from aqueous ethanol afforded *trans* : *trans*-matricarianol (II), m. p. and mixed m. p. 101—105° (see below).

Deca-trans-2 : trans-8-*diene*-4 : 6-*diyn*-1-*ol* (trans : trans-*Matricarianol*) (II).—This alcohol crystallised from aqueous ethanol or light petroleum as needles, m. p. 105·5—106·5° undepressed on admixture with synthetic material[4] or with the reduction product from the ester (I; R = Me). It had ultraviolet (see Table) and infrared absorption spectra identical with those of synthetic material (Found : C, 82·5; H, 7·0. Calc. for $C_{10}H_{10}O$: C, 82·2; H, 6·8%). Hydrogenation of the alcohol (II) (37 mg.) in ethanol over 2% palladium on calcium carbonate (50 mg.) gave an oil, converted directly into decyl 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 55—57°.

Methyl 10-*Hydroxydec*-trans-2-*ene*-4 : 6-*diynoate* (III; R = Me).—(*a*) Isolated as an almost colourless oil after low-temperature crystallisation from ether–light petroleum, the *ester* was characterised by its ultraviolet (cf. Table) and infrared absorption spectra. Hydrolysis of the ester (80 mg.) by the method used for (I; R = Me) gave, on crystallisation of the product from aqueous ethanol, 10-*hydroxydec*-trans-2-*ene*-4 : 6-*diynoic acid* (III; R = H) as plates, m. p. 154·5—156°; ultraviolet absorption spectrum, see Table (Found : C, 67·6; H, 6·0. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·7%). Hydrogenation of the acid (12 mg.) in ethanol over 2% palladium on carbon (20 mg.) gave a crystalline solid (11 mg.), which was oxidised by excess of 8N-chromic acid in acetone to sebacic acid, m. p. and mixed m. p. 128·5—132·5°.

(*b*) To a solution of cuprous chloride (17 g.) and ammonium chloride (2[illegible] g.) in water (85 c.c.) containing a little hydrochloric acid (pH *ca.* 3·5) were added methyl pent-*trans*-2-en-4-ynoate (1·6 g.) and pent-4-ynol (4·7 g.), followed by hydrogen peroxide (100 vol.; 30 c.c.) added dropwise during 1 hr. at 10°. The mixture was then acidified, and isolation with ether gave a semi-crystalline mixture (4·6 g.). Adsorption on alumina (400 g.) from benzene and elution with the same solvent gave a fraction containing the diester (IV; R = Me), and then one containing the desired hydroxy-ester (III; R = Me), purified by low-temperature crystallisation to constant

[10] Bu'Lock, Jones, Mansfield, Thompson, and Whiting, *Chem. and Ind.*, 1954, 990.

extinction coefficient; for ultraviolet absorption spectrum, see Table. The ultraviolet and infrared absorption spectra were identical with those of the naturally-derived compound. The hydroxy-ester was hydrolysed as described above to give the hydroxy-acid (III; R = H) which when recrystallised from aqueous ethanol had m. p. and mixed m. p. with naturally-derived material, 153—154° (ultraviolet absorption spectrum, see Table).

Deca-trans-2 : trans-8-*diene*-4 : 6-*diyne*-1 : 10-*dioic acid* (IV; R = H).—Precipitation from aqueous ethanol gave the acid as an amorphous powder, decomp. *ca.* 200°, characterised by its ultraviolet (see Table) and infrared absorption spectra and equivalent weight (potentiometric titration) [Found: equiv., 95. Calc. for $C_8H_4(CO_2H)_2$: equiv., 95]. Hydrogenation of the diacid (58 mg.) over platinum oxide (16 mg.) in ethanol, removal of catalyst and solvent, and recrystallisation of the product from water yielded sebacic acid, m. p. and mixed m. p. 130·5—133°. The dimethyl ester was isolated by chromatography of the mixed esters (cf. below) and also by methylation of (IV; R = H); the diacid (78 mg.) was dissolved in dry methanol containing 3% concentrated sulphuric acid and the solution set aside at 15° for *ca.* 40 hr., pale yellow plates separating. The mixture was diluted with water and extracted with ether; isolation of the neutral product and recrystallisation from ethanol yielded the diester (IV; R = Me) as plates, m. p. 104·5—107·5° (Found: C, 66·3; H, 4·6. Calc. for $C_{12}H_{10}O_4$: C, 66·1; H, 4·6%). The dimethyl ester, prepared by the method of Heilbron, Jones, and Sondheimer,[6] had m. p. 105·5—108·5° and was identical with the naturally derived material.

Dimethyl Octa-trans-2 : trans-6-*dien*-4-*yne*-1 : 8-*dioate* (C_8 *Diester*) (V; R = Me).—(*a*) Isolated from the esterified "acid fraction" (see below), this *diester* crystallised from light petroleum as plates, m. p. 117—119·5° (Found: C, 61·8; H, 5·5. $C_{10}H_{10}O_4$ requires C, 61·8; H, 5·2%); ultraviolet absorption spectrum, see Table. Hydrogenation of (V; R = Me) (14 mg.) in ethanol over 2% palladium on calcium carbonate (40 mg.), removal of catalyst and solvent, hydrolysis of the residual oil with potassium hydroxide in methanol, and isolation and crystallisation of the acidic product gave suberic acid, m. p. and mixed m. p. 140—142°.

(*b*) To a mixture of pent-*trans*-2-en-4-ynol (5·5 g.) and dihydropyran (6·0 g.), concentrated hydrochloric acid (0·05 c.c.) was added with cooling. The mixture was set aside at 20° for 16 hr., potassium hydroxide (*ca.* 0·1 g.) was added and the filtered mixture distilled to give 2-pent-2′-en-4′-yn-1′-yloxytetrahydropyran (9·8 g.), b. p. 45—47°/0·15 mm., n_D^{18} 1·4889. This (9·2 g.) in dry ether (10 ml.) was added to a stirred suspension of lithium amide (from 0·4 g. of lithium) in liquid ammonia through which a stream of nitrogen was passing. Epichlorohydrin (5·2 g.) was added dropwise and the mixture stirred under nitrogen for 7 hr. Ammonium chloride (3 g.) was added, the ammonia evaporated, and the residue extracted with ether. The ether-insoluble material was taken up in water, and the solution filtered to remove traces of gum and extracted with ether. The combined ether extracts were washed successively with dilute sulphuric acid, aqueous sodium carbonate, and water, dried (Na_2SO_4) and evaporated leaving a yellow oil (10 g.). This was dissolved in light petroleum–benzene (6 : 1) and adsorbed on alumina; elution with the same solvent yielded unchanged materials (6·4 g.) and elution with benzene yielded an oil (2·9 g.) which was hydrolysed in methanol (50 c.c.) containing sulphuric acid (0·2 c.c.). The solution was left overnight, sodium carbonate was added, and the filtered solution was evaporated. Low-temperature crystallisation from ether and recrystallisation from ether–light petroleum gave octa-*trans*-2 : *trans*-6-dien-4-yne-1 : 8-diol (0·4 g.), m. p. 78—81°, raised by further recrystallisation to 80—81·5°. The crude diol had been obtained previously by Heilbron *et al.*,[11] and has since been obtained crystalline by Bohlmann and Mannhardt,[12] who report m. p. 80—80·5°.

Oxidation of the diol (0·3 g.) with manganese dioxide in methylene chloride was incomplete and the partially oxidised material in acetone was treated with an excess of 8N-chromic acid in acetone. The mixture was worked to give an acid fraction containing a pale yellow solid (215 mg.). This was dissolved in methanol (50 c.c.) containing 3% by volume of concentrated sulphuric acid, and the mixture set aside at 20° for 44 hr. A neutral fraction (230 mg.) was obtained which, after chromatography on alumina, afforded the diester, m. p. and mixed m. p. 118—119°; ultraviolet spectrum, see Table; infrared spectrum identical with that of the naturally-derived material.

Dimethyl Dec-trans-2-*ene*-4 : 6-*diyne*-1 : 10-*dioate* (VI; R = Me).—(*a*) Isolated from the esterified acid fraction (see below) this diester had m. p. 56·5—58° (from light petroleum).

[11] Heilbron, Jones, Lacey, McCombie, and Raphael, *J.*, 1945, 77.
[12] Bohlmann and Mannhardt, *Chem. Ber.*, 1956, **89**, 1307.

(*b*) To a solution of the hydroxy-ester (III; R = Me) (94 mg.) in acetone (8 c.c.), 8N-chromic acid (0·25 c.c.) was added dropwise. After 5 min. the mixture was diluted with water and extracted repeatedly with ether. The combined ether extracts were extracted with aqueous sodium hydrogen carbonate, and this extract acidified and extracted with ether. Evaporation of the ether solution gave a solid (43 mg.), which was methylated to give the *diester* (VI; R = Me) (37 mg.), silky needles (from light petroleum), identical in m. p. (56·5—58°), mixed m. p., and ultraviolet (see Table) and infrared spectra with the naturally-derived compound (Found: C, 65·5; H, 5·6. $C_{12}H_{12}O_4$ requires C, 65·4; H, 5·5%).

Deca-trans-2 : trans-8-*diene*-4 : 6-*diynyl* *Deca*-trans-2 : trans-8-*diene*-4 : 6-*diynoate* (VII).—(*a*) This *ester* was isolated as described below, forming needles, m. p. 124—126° (Found: C, 83·6; H, 5·9. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·6%); for ultraviolet absorption spectrum, see Table and Fig. 2.

(*b*) Deca-*trans*-2 : *trans*-8-diene-4 : 6-diynoic acid (I; R = H) (35 mg.) was treated with thionyl chloride (*ca.* 0·3 c.c.) with slight warming until the acid dissolved; after 30 min. at 20°, excess of thionyl chloride was distilled off under reduced pressure. To the yellow residue was added a solution of deca-*trans*-2 : *trans*-8-diene-4 : 6-diyn-1-ol (II) (34 mg.) in dry pyridine (0·4 c.c.); the mixture was left overnight at 0°, then diluted with water and extracted with ether. The combined ether extracts were washed successively with aqueous sodium hydrogen carbonate, water, dilute hydrochloric acid, and water, dried ($MgSO_4$), and evaporated. The residue (50 mg.) was dissolved in light petroleum and purified by chromatography on a short column of alumina, followed by recrystallisation from the same solvent, to give needles, m. p. and mixed m. p. 124·5—126°, with ultraviolet and infrared absorption spectra identical with those of the natural ester.

Methyl 10-(*Deca*-trans-2 : trans-8-*diene*-4 : 6-*diyn*-1-*oyloxy*)-*dec*-trans-2-*ene*-4 : 6-*diynoate* (VIII).—(*a*) This diester, isolated as described below, crystallised from light petroleum as plates, m. p. 91—93° (Found: C, 75·5; H, 5·7. $C_{21}H_{18}O_4$ requires C, 75·4; H, 5·4%); for ultraviolet absorption spectrum see Table and Fig. 3.

(*b*) Reaction of the acid chloride from deca-*trans*-2 : *trans*-8-diene-4 : 6-diynoic acid (93 mg.) with the hydroxy-ester (III; R = Me) (72 mg.) and purification of the product as described for (VII) gave the required diester (VIII) as plates, m. p. and mixed m. p. 91—94°, having ultraviolet and infrared absorption spectra identical with those of the natural material.

Extraction and Separation of the Components.

Because of the varying composition of extracts it is impossible to describe a generally applicable procedure; moreover, crude fractions and mother liquors from several runs were often combined and worked up together. The following account, summarised in the flow-sheet, describes the extraction and working-up of a batch of 16 cultures taken 68 days after inoculation.

The culture medium (*ca.* 10 l.) was extracted with ether (5 × 1 l.) and the mycelium extracted continuously (48 hr.) with ether. The extracts were each divided into an acidic and a neutral fraction by extraction with saturated aqueous sodium hydrogen carbonate; the neutral fractions were kept separate whilst the bicarbonate extracts were combined, acidified, and extracted with ether to give a single acid fraction.

Neutral Fraction from the Medium.—Evaporation yielded yellow oil and solid (850 mg.) which was adsorbed on alumina (150 g.) from 1 : 4 light petroleum–benzene. Elution with the same solvent gave successively three main fractions with longest-wave absorption maxima respectively at *ca.* 3350 (" A "), 3130 (" B "), and 3050 Å (" C ").

Fraction " A " gave an oil (140 mg.) which was separated by chromatography on alumina (25 g.) and elution with light petroleum, into two fractions having the ultraviolet spectra of esters (I) and (IV), respectively. Evaporation of the first fraction gave a yellow oil (105 mg.) which, when treated with a few drops of ethanol and set aside at 0°, yielded *trans*: *trans*-matricaria ester (I; R = Me) (12 mg.) as needles, m. p. 60—63° (after two recrystallisations from aqueous ethanol). The second fraction gave crystals (11 mg.) from which ester (IV; R = Me), m. p. 106·5—110°, was obtained after two recrystallisations from alcohol.

Removal of solvent from fraction " B " and three recrystallisations from ethanol gave *trans* : *trans*-matricarianol (II), as needles (64 mg.), m. p. 105—107°. Similarly, fraction " C " afforded the hydroxy-ester (III) as a yellow oil, low-temperature crystallisation of which from ether–light petroleum gave an almost colourless oil (52 mg.) with $\varepsilon = 20{,}200$ at 3050 Å.

Neutral Fraction from the Mycelium.—Evaporation of the ether yielded a yellow oily solid

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(2·7 g.). Trituration with benzene left a white residue (*ca.* 1 g.) which gave a positive Liebermann–Burkhardt test and an ultraviolet spectrum suggesting that it contained eburicoic and dehydroeburicoic acids.[3]

Evaporation of the benzene afforded a mixture (1·48 g.) of oil and crystals which was dissolved in light petroleum–benzene (1 : 2) and adsorbed on alumina (200 g.). Elution with the same solvent gave three successive fractions with longest-wavelength ultraviolet absorption maxima respectively at 3350 (" D "), 3470 (" E "), and 3130 Å (" F "). Further elution with benzene gave a fourth fraction (" G ") with longest-wavelength ultraviolet absorption maximum at 3050 Å.

Removal of solvent from " D " yielded pale yellow crystals (880 mg.), which were adsorbed from light petroleum on to alumina (200 g.). Elution with light petroleum gave, first, a fraction containing *trans* : *trans*-matricaria ester (I; R = Me), m. p. 63—64° (460 mg.; after three recrystallisations from light petroleum). Immediately thereafter was eluted a fraction having ultraviolet absorption (Fig. 2) corresponding to a mixture of (I) and *trans* : *trans*-matricarianol (II), evaporation of which yielded the ester (VII) as needles, m. p. 125—127·5° (8 mg., after three recrystallisations from ethanol). Elution with benzene–light petroleum (1 : 1) gave a fraction affording the diester (IV), which formed plates, m. p. 107—110° (3 mg., after three recrystallisations from light petroleum). Continued elution with the same solvent then gave a fraction containing (IV) mixed with other diesters (longest-wavelength ultraviolet absorption maximum at 3050 Å; 10 mg. of yellow gum and crystals), which was not worked up (cf. working up of the acid fraction below), followed by a fraction with ultraviolet absorption (Fig. 3) corresponding to a mixture of esters (I; R = Me) and (III; R = Me). Evaporation gave a gum which crystallised on trituration with light petroleum affording ester (VIII) as prisms, m. p. 92—94° (4 mg., after three recrystallisations from light petroleum).

Evaporation of " E " gave a yellow gum (9 mg.); the ultraviolet absorption of this material showed a single broad maximum at *ca.* 3470 Å; its infrared spectrum contained a strong band at 1660 cm.$^{-1}$ and no band attributable to C≡C, CH=C=CH, or *trans*-CH=CH groups.

Evaporation of " F " yielded pale yellow crystals (34 mg.). Repeated recrystallisation of this material from aqueous ethanol gave plates (4 mg.), m. p. 138—147°, of a compound showing ultraviolet and infrared absorption spectra similar to those of ergosterol. From the mother-liquors was isolated *trans* : *trans*-matricarianol (II) (13 mg.), m. p. 103—107° (from light petroleum).

Evaporation of " G " gave a yellow gum (24 mg.) containing (by spectroscopic assay) *ca.* 14 mg. of the hydroxy-ester (III).

Total Acid Fraction.—Evaporation of the combined acid fractions gave a yellow-brown gum (600 mg.). This was esterified with methanolic sulphuric acid, and the neutral ester fraction (400 mg.) was adsorbed on alumina (100 g.) from benzene–light petroleum (1 : 1); elution with the same solvent and evaporation gave a crystalline " ester + diester " fraction (see below). Elution with benzene gave a fraction containing the hydroxy-ester (III; R = Me) (*ca.* 20 mg., assayed spectroscopically).

The " ester + diester " fraction (106 mg.) was adsorbed on alumina (30 g.) from light petroleum; elution with the same solvent yielded eight successive fractions " K—R." Fraction " K," a gum (10 mg.), showed no distinctive ultraviolet absorption. " L " contained an oil (3·5 mg.) showing the ultraviolet absorption spectrum of matricaria ester modified by that of a component with absorption maxima at 2850 and 3050 Å, probably therefore a conjugated diynene ester. " M " contained crude *trans* : *trans*-matricaria ester (I; R = Me) (5 mg.), identified by its infrared absorption spectrum; " N " gave a gum (4 mg.) containing the ester (I; R = Me) together with material having the ultraviolet absorption spectrum of an ene-diyne; " O " gave crystalline diester (IV), m. p. 90—107° (2 mg., after two recrystallisations from light petroleum). " P " gave a crystalline mixture (10·5 mg.) of (IV) with dimethyl octa-*trans*-2 : *trans*-6-dien-4-ynedioate (V); " Q " consisted mainly of the latter compound, m. p. 117—119° (15 mg., after two recrystallisations). Fraction " R " (4 mg.) consisted mainly of the diester (VI; R = Me).

Some different procedures used with other batches may be noted. When the acid fraction was rich in the dibasic acid (IV; R = H) some of this could be isolated by deposition from ethanol before the esterification. In the fractionation of the " esters + diesters " mixture, the fractions containing the diester (IV; R = Me) and the diester (V; R = Me) were efficiently resolved by crystallisation from carbon disulphide, in which (V) is less soluble. When larger

fractions composed mainly of the hydroxy-ester (III; R = Me) were purified by re-chromatography, a small fraction was obtained with ultraviolet absorption corresponding to that of (III; R = Me) together with a compound with a spectrum of matricaria ester type; this is the component presumed to be the as-yet-unknown hydroxy-ester (IX).

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THE UNIVERSITY, MANCHESTER, 13.
THE DYSON PERRINS LABORATORY, OXFORD. [*Received, November 8th*, 1956.]

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309. *The Chemistry of Nitrosyl Complexes. Part III.* Evidence for Compound Formation in Liquid Nitrosyl Chloride from Tracer Studies.*

By J. LEWIS and D. B. SOWERBY.

The rapid exchange of ^{36}Cl between the nitrosyl chloride addition compounds of ferric chloride and antimony pentachloride with liquid nitrosyl chloride is in agreement with the formulation of these compounds as nitrosonium salts. With the more covalent chlorides, arsenic trichloride, phosphorus oxychloride, and carbon tetrachloride, exchange is rapid with arsenic trichloride but very slow with phosphorus oxychloride and carbon tetrachloride. Phase studies indicate the formation of a compound, $AsCl_3,2NOCl$, between arsenic trichloride and nitrosyl chloride but no compound formation between phosphorus oxychloride and nitrosyl chloride. The rapid exchange of ^{36}Cl between arsenic trichloride and nitrosyl chloride is attributed to the formation of this compound which behaves as a very weak electrolyte in the nitrosyl chloride solvent system.

The slow exchange of nitrosyl chloride with the non-electrolyte phosphorus oxychloride being assumed to occur through the presence of free chloride ions, the free chloride-ion concentration in nitrosyl chloride is calculated to be 10^{-8} g.-ion $l.^{-1}$, and the ionic product $[NO^+][Cl^-] = 10^{-16}$ g.-ion^2 $l.^{-2}$.

PREVIOUS studies in nitrosyl chloride have been mainly concerned with the behaviour of strong electrolytes [1] formed by the reaction of metal chlorides with the solvent. Thus complex formation occurs between nitrosyl chloride and ferric chloride to give the strong electrolyte nitrosonium tetrachloroferrite; and with antimony pentachloride to give nitrosonium hexachloroantimonate. The formation of these ionic compounds should lead to rapid exchange of ^{36}Cl between ferric chloride and antimony pentachloride and the solvent.

From the general behaviour in other systems, we would expect that arsenic trichloride and phosphorus oxychloride would behave as either weak or non-electrolytes in nitrosyl chloride. We have, therefore, studied the general properties of such solutions, with particular reference to the influence of the nature of the solute on the exchange of labelled chlorine. It was of interest to see if weaker compound formation also led to rapid exchange of chlorine with the solvent.

EXPERIMENTAL

Preparation of Compounds containing ^{36}Cl.—Radioactive nitrosyl chloride was prepared as described in Part II.

* Part II, *J.*, 1956, 150.

[1] Burg and Campbell, *J. Amer. Chem. Soc.*, 1948, **70**, 1954; Burg and McKenzie, *ibid.*, 1952, **74**, 3143.

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Nitrosonium hexachloroantimonate. Radioactive nitrosyl chloride was condensed on a block of antimony metal cooled to −40°. The temperature was allowed to rise slowly, and reaction started. At room temperature, the excess of antimony was removed, leaving the yellow complex $NOCl,SbCl_5$ (Found : Cl, 58·6. Calc. for $NOSbCl_6$: Cl, 58·4%).

Arsenic trichloride. Radioactive tetramethylammonium chloride [2] (0·2 g.) was dissolved in anhydrous arsenic trichloride (10 ml.). Rapid exchange occurred [3] and arsenic trichloride, containing ^{36}Cl, was distilled as required.

Phosphorus oxychloride. Radioactive tetraethylammonium chloride was dissolved in phosphorus oxychloride, and active phosphorus oxychloride was distilled as required.

Other Compounds.—(i) Carbon tetrachloride was dried ($CaCl_2$) and fractionally distilled immediately before use. (ii) Anhydrous ferric chloride was prepared by passing dry chlorine over heated iron wire. The product was sublimed into small ampoules in a stream of chlorine, and absorbed chlorine was removed under reduced pressure. The ampoules were sealed in a stream of nitrogen.

Exchange Runs.—The apparatus and techniques employed were those described previously.[2] Solid samples packed in small glass tubes open at both ends were added to the exchange vessel; with liquids, additions were made from a microburette. The burette was fitted with standard ground-glass joints for attachment to the exchange vessel. Activities were determined by precipitating the chloride as silver chloride and counting on G.E.C. 1·5 cm. planchets, with samples of infinite thickness.

In the experiments, inactive ferric chloride and carbon tetrachloride were employed with active nitrosyl chloride. For exchanges with antimony pentachloride, arsenic trichloride, and phosphorus oxychloride, active chlorides were used with inactive nitrosyl chloride.

A detailed study of the slow exchange between phosphorus oxychloride and nitrosyl chloride was carried out. The components were mixed and fractions were sealed in phials, which were allowed to attain 18°. After various intervals, a phial was broken, and the nitrosyl chloride allowed to evaporate. After complete removal of the nitrosyl chloride the activity of the chlorine in the remaining phosphorus oxychloride was determined. For 0·2404M-phosphorus oxychloride solution, the percentage exchange after 0, 14, and 33 days was 0, 20·6, and 40·6, respectively.

Phase Studies.—The freezing points of mixtures of phosphorus oxychloride–nitrosyl chloride and arsenic trichloride–nitrosyl chloride were determined by the warming-curve technique.[4] Thermometers were calibrated against the m. p. of ice, carbon tetrachloride, mercury, and chlorobenzene, and the sublimation point of solid carbon dioxide.

Conductivity Measurements in Liquid Nitrosyl Chloride.—The conductivities of arsenic trichloride, phosphorus oxychloride, and chloroform were determined in liquid nitrosyl chloride at −20°. The cell used was that described previously,[3] and measurements were made with a Mullard conductivity bridge, type E 7566. A solution of the required liquid, in liquid nitrosyl chloride, was prepared in the cell by use of a weight pipette, and liquid nitrosyl chloride was added from a burette, designed to enable nitrosyl chloride to be maintained at −20° for long periods. This was attained by surrounding the burette with a glass envelope through which was circulated cold alcohol. The following Table contains the equivalent conductivities of the liquids in nitrosyl chloride.

Compound								
$POCl_3$	Spec. conductivity (ohm^{-1} $cm.^2$)	0·173	0·194	0·208	0·220	0·230	0·240	0·242
	10^2 × concn. (mole $l.^{-1}$)	3·32	3·02	2·77	2·56	2·38	2·22	2·08
$AsCl_3$	Spec. conductivity (ohm^{-1} $cm.^2$)	0·204	0·220	0·228	0·282	0·314	0·347	0·402
	10^2 × concn. (mole $l.^{-1}$)	2·86	2·65	2·47	2·06	1·85	1·68	1·48
$CHCl_3$	Spec. conductivity (ohm^{-1} $cm.^2$)	0·104	0·111	0·119	0·126	0·133	0·140	0·148
	10^2 × concn. (mole $l.^{-1}$)	3·79	3·53	3·31	3·13	2·95	2·79	2·65

These values indicate that arsenic trichloride is a slightly better conductor than phosphorus oxychloride : the values for chloroform solutions were variable and the observed conductivity in the chloroform may well be associated with traces of impurity.

Conductometric Titration.—Arsenic trichloride was titrated with tetraethylammonium chloride in liquid nitrosyl chloride at −20°, an apparatus similar to that described for the

[2] Lewis and Wilkins, *J.*, 1955, 56.
[3] Lewis and Sowerby, *J.*, 1957, 336.
[4] Addison, Conduit, and Thompson, *J.*, 1951, 1303.

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conductivity study being used. Fig. 1 shows the portion of the curve of the variation in conductivity of solutions of arsenic trichloride on addition of tetraethylammonium chloride, over the concentration range of the 1 : 1 compound. No breaks were observed at higher molecular ratios of the components, the conductivity rising smoothly with addition of tetraethylammonium chloride.

Electrolysis of Arsenic Trichloride in Liquid Nitrosyl Chloride.—The electrolysis was carried out in an apparatus similar to that used by Burg and McKenzie.[1] The electrodes were platinum cylinders, 4·5 cm. long and 0·7 cm. in diameter, and the electrolysis was carried out at −20° for 20 hr. The contents of the centre compartment were then frozen by liquid oxygen, and the anode and cathode fractions were removed. The concentration of arsenic in the former was always greater than that in the latter :

e.g., concn. of As in anode compartment = 0·0070 g./ml.
,, ,, ,, cathode compartment = 0·0045 g./ml.

Owing to the low conductivity of these solutions, it was not possible to determine transport numbers, as the distance between the electrodes was not sufficient to ensure that there was no concentration change in the solution separating the anode and the cathode compartment.

Discussion

Ferric chloride dissolves readily in nitrosyl chloride to give a highly conducting solution and behaves as a strong electrolyte in the system. The solutions are considered to contain nitrosonium chloroferrite, and on evaporation of the solvent, a solid of composition $FeCl_3$,NOCl can be isolated. Tensimetric studies indicate that, in addition to the monosolvate, ferric chloride exists in solution as a disolvated molecule. Magnetic studies on these solutions show that the probable structure of such a complex involves solvation of the nitrosonium ion, and not further addition of chloride ion to the ferric ion.[1] The tetrachloroferrite ion may be expected to be labile with respect to chloride-ion exchange, and this exchange is analogous to the exchange of labelled water molecules with metal aquo-complexes in water. These exchanges are normally rapid. Antimony pentachloride behaves in a similar manner, reacting with nitrosyl chloride to yield nitrosonium chloroantimonate. In many cases, the formulation of the compounds as salts containing an ion characteristic of the solvent is based on the isolation of a compound containing solvent molecules and the enhanced conductivity of the solvent on addition of the metal chloride. Huston [5] has recently thrown doubt on this type of formulation. Aluminium chloride dissolves in carbonyl chloride to give a conducting solution and forms a monosolvate that was formulated as $(COCl)^+(AlCl_4)^-$. Huston observed, however, that the exchange of labelled chlorine between aluminium chloride and carbonyl chloride was slow. A structure, as suggested above, for the complex would have led to a rapid exchange of chlorine between the aluminium chloride and the solvent.

The Table contains typical values for the exchange of labelled chlorine (^{36}Cl) between nitrosyl chloride and some soluble chlorides, and in agreement with the formulation above, ferric chloride and antimony pentachloride are exchanged completely within the time of separation. An interesting difference arises in the behaviour of the more covalent chlorides, for arsenic trichloride is exchanged rapidly with nitrosyl chloride but phosphorus oxychloride and carbon tetrachloride only very slowly. We have investigated the physical properties of solutions of arsenic trichloride and phosphorus oxychloride in liquid nitrosyl chloride to determine if the difference in the rates of exchange can be attributed to any major difference in the behaviour of such solutions.

Thermal Measurements.—With ionic chlorides, arsenic trichloride forms stable, solid compounds involving the tetrachloroarsenite ion,[6] $(AsCl_4)^-$, whereas phosphorus oxychloride normally solvates the chloride ion in solution but no solid derivatives of the corresponding ion, $(POCl_4)^-$, are known.[7] We would, therefore, expect that, if compound

[5] Huston, *J. Inorg. Nuclear Chem.*, 1956, **2**, 128.
[6] Gutmann, *Z. anorg. Chem.*, 1951, **266**, 331.
[7] *Idem, ibid.*, 1952, **270**, 179.

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formation involved such ions, it would be more pronounced in the case of arsenic trichloride. Fig. 2 shows the liquidus curves for mixtures of arsenic trichloride and phosphorus oxychloride with nitrosyl chloride. The solutions are miscible over the whole concentration range. With phosphorus oxychloride, a simple eutectic was observed at −74°, with a composition of 78 moles % of nitrosyl chloride, showing the absence of any compound formation between the components. However, with arsenic trichloride, a maximum is found at a concentration of 68 moles % of nitrosyl chloride, indicating that a compound, with a molecular composition $2NOCl,AsCl_3$, is formed. There was no apparent break in the curve at the 1 : 1 mole ratio. The shape and height of the maximum suggest that the compound has not a very great stability, and is probably highly dissociated. This compound may be considered either as a weak addition compound or as an ionic compound analogous to the chloroferrite addition compound discussed above. In the formulation

FIG. 1.

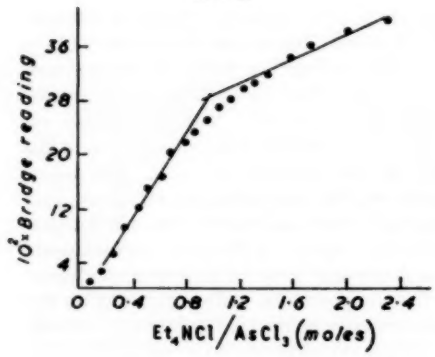
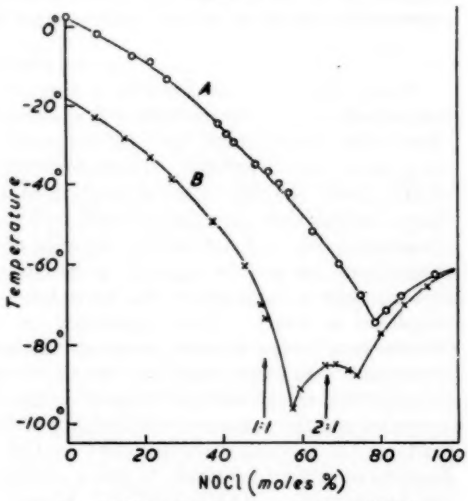


FIG. 2.



A = $POCl_3$ + NOCl. B = $AsCl_3$ + NOCl.

as an ionic compound, the structure may be either $[(NO)(NOCl)]^+[AsCl_4]^-$ (I) or $(NO)_2^+(AsCl_5)^{2-}$ (II). Structure (I) involves the solvation of the nitrosonium ion, in a similar manner to that postulated for nitrosonium chloroferrite. In agreement with this structure is the fact that even the most strongly donating chloro-compounds only give a tetrachloroarsenite ion in arsenic trichloride solutions. Consistently with structure (II), a phase study of the aluminium chloride–nitrosyl chloride system shows that aluminium chloride gives two complexes [8] with molecular compositions $AlCl_3,NOCl$ and $AlCl_3,2NOCl$. The disolvate, which is formulated as a solvated nitrosonium derivative, is much more unstable than the monosolvate and is found to have an incongruent m. p. at 17·5°. Thus, if structure (I) is correct, we would have expected some indication of the formation of a monosolvate in the phase diagram, although the larger size of the ion $[AsCl_5]^{2-}$ than of the ion $[AlCl_4]^-$ may account for the increased stability of a compound of structure (I).

Electrochemical Studies.—The conductivities of solutions of phosphorus oxychloride and arsenic trichloride in liquid nitrosyl chloride indicate that these liquids behave as either very weak electrolytes or non-electrolytes. The values of the equivalent con-

[8] Houtgraaf and de Roos, *Rec. Trav. chim.*, 1953, **72**, 963.

ductivities of these solutions do not differ significantly from those of solutions of chloroform, which may be considered to be a non-electrolyte in this system. The high degree of dissociation of the arsenic trichloride complex, deduced from the phase diagram, therefore probably involves dissociation into nitrosyl chloride and arsenic trichloride rather than

Exchange of radio-chlorine between nitrosyl chloride and some soluble chlorides.

Solute	Conditions	Time of contact (min.)	Activity of NOCl (counts/min.)	Value for 100% exchange (counts/min.)
$NOFeCl_4$	−20°, in dark	2½	144	146
		3½	140	
		70	143	
$NOSbCl_6$	−20°, in light	6	135	132
		11	134	
		25	136	
		56	138	
$AsCl_3$ ...	−20°, in light	5	269	265
		28	274	
		51	274	
		91	265	
	−20°, in dark	5	132	134
		20	137	
$POCl_3$ ...	−20°, in light	5	3	140
		50	2	
		75	2	
	−20°, in dark	60	0	134
		100	1	
		285	0	
CCl_4 ...	−30°, in light	8	292 *	161
		42	302	
		75	293	
		98	289	

* Original NOCl = 302 counts/min.

into ionic components. A conductometric titration between arsenic trichloride in liquid nitrosyl chloride and a strong base in the nitrosyl chloride solvent system, tetraethylammonium chloride, gave a break in the conductivity curve at a molecular ratio of $Et_4NCl : AsCl_3 = 1 : 1$. No break occurred at any other concentration. Phosphorus oxychloride under similar conditions gave no break in the conductivity curve. This may be taken to indicate that, in nitrosyl chloride, arsenic trichloride forms a monobasic acid, which may be considered as $[(NO)(NOCl)]^+[AsCl_4]^-$, whilst phosphorus oxychloride is probably a non-electrolyte. An electrolysis of a solution of arsenic trichloride in nitrosyl chloride between nickel or platinum electrodes also agreed with the arsenic's being present in the anion, as arsenic concentrated in the anode compartment.

The exchange of labelled chlorine between nitrosyl chloride and arsenic trichloride may then occur by the formation of this weak addition compound, whilst phosphorus oxychloride, which does not form a similar compound, may be expected to be exchanged slowly.

The bimolecular rate constant for the exchange of phosphorus oxychloride with chloride ion in acetonitrile has been determined over a temperature range,[3] and at 18° the calculated rate constant is 66 sec.$^{-1}$ mole^{-1} l. If we assume that the exchange between phosphorus oxychloride and nitrosyl chloride occurs by a similar bimolecular process involving chloride ion (present owing to the self-dissociation of liquid nitrosyl chloride), we can calculate the chloride-ion concentration in liquid nitrosyl chloride. The rate of the phosphorus oxychloride–nitrosyl chloride exchange reaction is given by

$$R = \frac{0{\cdot}693}{t_{\frac{1}{2}}} \cdot \frac{3[POCl_3][NOCl]}{[3[POCl_3] + [NOCl]]}$$

and if we assume the above bimolecular mechanism, $R = k_2[POCl_3][Cl^-]$ where k_2 is the rate constant and $[Cl^-]$ is the concentration of chloride ion due to the self-ionisation of nitrosyl chloride. This requires that the rate constant, k_2, is the same as that in acetonitrile. Normally, for a bimolecular mechanism, involving an ion and a neutral molecule, the rate constant is slightly increased on decrease of the polarity of the solvent, and therefore the concentration of free chloride ion in nitrosyl chloride will probably be lower than this calculated value. As phosphorus oxychloride is a non-electrolyte in this system, we

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may then consider that the concentration of nitrosonium ion is equal to the concentration of chloride ion. Hence, the ionic product for nitrosyl chloride $K = [NO^+][Cl^-]$ will reduce to $K = [Cl^-]^2$. From the above data, the chloride-ion concentration in nitrosyl chloride at 18° is 10^{-8} g.-ion $l.^{-1}$ and the ionic product is 10^{-16} g.-ion^2 $l.^{-2}$.

One of us (D. B. S.) thanks the University of Sheffield for the award of a Robert Styring Scholarship during the tenure of which this research was carried out.

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310. *Lipids. Part V.* Total Synthesis of Ximenynic Acid, Homoricinstearolic Acid, and Two Fatty Hydroxy-acids with Allenic Side-branches.*

By L. CROMBIE and A. G. JACKLIN.

Ximenynic (octadec-*trans*-11-en-9-ynoic) acid (VII) is synthesised from dec-3-en-1-yne by chain extension with 1-chloro-7-iodoheptane, followed by nitrile synthesis, and is identical with the natural substance. A preparative sequence making 1-chloro-7-iodoheptane more accessible is reported.

Methyl and ethyl 11-bromoundec-9-ynoate and methyl 12-bromododec-10-ynoate are prepared by a formaldehyde coupling procedure, and their behaviour in Reformatski reactions with *n*-heptaldehyde is examined. Methyl 12-bromododec-10-ynoate gives a mixture of 11-hydroxy-10-vinylideneheptadecanoic acid (XVII) and 13-hydroxynonadec-10-ynoic (homoricinstearolic) acid (XIX) in the proportion 7 : 3 (by infrared analysis); the two are separated by clathrate formation with urea. The structure of the allenic acid (XVII) is established by degradation to formaldehyde and 11-hydroxy-10-oxoheptadecanoic acid: with lead tetra-acetate the latter gives heptaldehyde and sebacic acid. Spectroscopic results are in agreement. 10-Hydroxy-9-vinylidenehexadecanoic acid is prepared by a similar route. The method is more useful for preparing hydroxy-acids with allenic side-branches than for the synthesis of ricinstearolic acid and related substances.

XIMENYNIC (santalbic) acid was first recognised in Nature by Ligthelm and Schwartz [1] but it is now known to occur in a number of seed fats of the genera *Ximenia* and *Santalum*.[2,3] Its structure, octadec-11-en-9-ynoic acid (VII), emerges from the following facts.[4] It can be hydrogenated to stearic acid with absorption of three mols. of hydrogen, the ultraviolet absorption suggests an enyne chromophore (which is confirmed since addition of one mol. of hydrogen over a poisoned catalyst increases the extinction coefficient), and on ozonolysis it gives *n*-heptaldehyde and azelaic acid. Ozonolysis establishes the orientation of the enyne system in the chain. Other data support the structure.[3,4] Three facts show that it has the *trans*-configuration: it is not stereomutated when heated with selenium,[4] it has a strong absorption band [5] at 955 $cm.^{-1}$, and when hydroxylated with performic acid and then hydrogenated it gives *erythro*-11 : 12-dihydroxystearic acid.[3]

Since ximenynic acid can be obtained by dehydrating (+)-ricinstearolic acid,[6,7] and since (±)-ricinstearolic acid was synthesised in Part II, a formal total synthesis has already been achieved.[7] Nevertheless, in order to develop a bridge between methods suitable for the synthesis of ricinoleic acid and those for elaeostearic acid, we have undertaken a direct total synthesis. In the synthesis of ricinoleic acid,[7] a terminal yn-β-ol system was first

* Part IV, *J.*, 1957, 479.

[1] Ligthelm and Schwartz, *J. Amer. Chem. Soc.*, 1950, **72**, 1868.
[2] Hatt and Szumer, *Chem. and Ind.*, 1954, 962; Ligthelm, Horn, Schwartz, and von Holdt, *J. Sci. Food Agric.*, 1954, **5**, 281; Hatt and Schoenfeld, *ibid.*, 1956, **7**, 130.
[3] Gunstone and Russell, *J.*, 1955, 3782.
[4] Ligthelm, Schwartz, and von Holdt, *J.*, 1952, 1088.
[5] Ahlers and Ligthelm, *J.*, 1952, 5039.
[6] Grigor, MacInnes, McLean, and Hogg, *J.*, 1955, 1069.
[7] Crombie and Jacklin, *Chem. and Ind.*, 1954, 1197; *J.*, 1955, 1740.

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constructed, the hydroxyl function was protected, the chain extended by a $\cdot[CH_2]_6\cdot I$ unit, and elaboration continued by malonate synthesis and removal of the tetrahydropyranyl protective grouping. (±)-Ricinoleic acid was finally produced by semihydrogenation. There are objections to this sequence when thermally sensitive systems are carried in the centre of the molecule and we have, therefore, avoided the malonate procedure in the synthesis of ximenynic acid.

Reformatski reaction between heptaldehyde and propargyl bromide gave the customary mixture of dec-1-yn-4-ol (I) and deca-1 : 2-dien-4-ol [7] which was converted into the toluene-*p*-sulphonyl derivative (II). Attempted deacylation with 30% aqueous potassium hydroxide was ineffective but sodium *n*-butoxide in butanol or, better, sodamide in liquid ammonia, was satisfactory,[8] the latter giving a 79% yield of dec-3-en-1-yne (III). The infrared spectrum of dec-3-en-1-yne showed no allenic contaminant and the presence of a substantial band at 952 cm.$^{-1}$ suggests that it is largely *trans*,[9] though it is not possible to assert that *cis*-material is absent. The synthesis is thus not stereospecific.

(I) $Me\cdot[CH_2]_5\cdot CH(OH)\cdot CH_2\cdot C{\equiv}CH \longrightarrow Me\cdot[CH_2]_5\cdot CH(OTs)\cdot CH_2\cdot C{\equiv}CH$ (II) $\longrightarrow$

(III) $Me\cdot[CH_2]_5\cdot CH{=}CH\cdot C{\equiv}CH \longrightarrow Me\cdot[CH_2]_5\cdot CH{=}CH\cdot C{\equiv}C\cdot[CH_2]_7\cdot Cl$ (IV) $\longrightarrow$

(VI) $Me\cdot[CH_2]_5\cdot CH{=}CH\cdot C{\equiv}C\cdot[CH_2]_7\cdot CN \longrightarrow Me\cdot[CH_2]_5\cdot CH{=}CH\cdot C{\equiv}C\cdot[CH_2]_7\cdot CO_2H$ (VII)

Ts = p-$C_6H_4Me\cdot SO_2$

To permit insertion of the carboxylic group by nitrile or Grignard synthesis, 1-chloro-7-iodoheptane was needed as chain extender. Though Huber has made use of it on one occasion,[10] the substance has been little used in fatty acid syntheses, presumably because expensive pimelic acid is needed for preparation of heptane-1 : 7-diol by his lithium aluminium hydride route. The synthesis shown, however, makes heptane-1 : 7-diol readily accessible in batches of 100 g. or more. Pent-4-yn-1-ol (IX), prepared by treating tetrahydrofurfuryl chloride (VIII) with sodamide in liquid ammonia,[11] is converted into the tetrahydropyranyl ether (X) and the chain extended with ethylene oxide [12] to give 7-2′-tetrahydropyranyloxyhept-3-yn-1-ol (XI). Removal of the tetrahydropyranyl residue and hydrogenation with Raney nickel gives heptane-1 : 7-diol in an overall yield of 59% (74% conversion of material) from the chloride (VIII). Heptane-1 : 7-diol can be satisfactorily converted into the iodochloride *via* the dichloride.[10] When the hydrogenation was carried out over palladium–barium sulphate at atmospheric pressure, considerable amounts of *n*-heptanol and undistillable material were formed. Though partial hydrogenolysis is the rule for 2-ethylenic alcohols it has generally been thought unusual for 3-acetylenic or ethylenic alcohols. However, we have previously encountered hydrogenolysis under similar conditions with this catalyst (6-methyloct-3-en-1-ol gives 3-methyloctane),[13] so it may be met in other instances.

$Cl\cdot CH_2\cdot CH(O)\cdot CH_2\cdot CH_2\cdot CH_2$ (VIII) $\longrightarrow HC{\equiv}C\cdot[CH_2]_3\cdot OH$ (IX) $\longrightarrow$

$HC{\equiv}C\cdot[CH_2]_3\cdot OPy$ (X) $\longrightarrow HO\cdot[CH_2]_2\cdot C{\equiv}C\cdot[CH_2]_3\cdot OPy$ (XI) $\longrightarrow HO\cdot[CH_2]_7\cdot OH$ (XII)

Py = 2-tetrahydropyranyl.

When treated with 1-chloro-7-iodoheptane, sodiodec-3-en-1-yne (cf. III) in liquid ammonia gave 17-chloroheptadec-7-en-9-yne (IV) in 65% yield. The latter was heated

[8] Eglinton and Whiting, *J.*, 1950, 3650.
[9] Allan, Meakins, and Whiting, *J.*, 1955, 1874.
[10] Huber, *J. Amer. Chem. Soc.*, 1951, **73**, 2730.
[11] Eglinton, Jones, and Whiting, *J.*, 1952, 2873.
[12] Cf. Raphael and Roxburgh, *J.*, 1952, 3875; and ref. 24.
[13] Crombie and Harper, *J.*, 1950, 2685.

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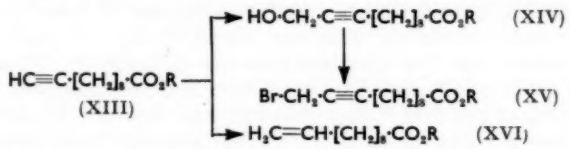
with sodium iodide and sodium cyanide in ethanol and, without isolation, the nitrile (VI) was hydrolysed to ximenynic acid (VII). This product was purified by formation of the urea clathrate compound and was obtained crystalline. It absorbed three mols. of hydrogen to give stearic acid and had the spectroscopic properties of a *trans*-enyne. Mixed m. p. and infrared comparisons showed it to be identical with the natural acid. Any *cis*-impurity in the intermediates must have been removed during purification.

Our opinion of the malonate reaction for syntheses of this type was confirmed by converting sodiodec-3-en-1-yne into 16-chlorohexadec-7-en-9-yne by reaction with 1-chloro-6-iodohexane. The unsaturated chloride was heated with sodium iodide in acetone and then used in the malonate reaction. After hydrolysis and decarboxylation there was little distillable product and the latter showed no enyne absorption.

We now deal with another approach to acids of the ricinstearolic and ximenynic type. This employs a Reformatski reaction with compounds of the type $Br{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}[CH_2]_n{\cdot}CO_2R$, where $n = 7$ or 8 and R = Et or Me, and is potentially capable of reducing the number of synthetic stages. Nevertheless, we expected difficulties because many reactions of 2-acetylenic halides lead to mixtures of allenes and acetylenes.[14,15] This is encountered in the Reformatski reaction between propargyl bromide and an aldehyde (above and Part II), as was originally pointed out by Wotiz,[15] but it is not a source of serious difficulty because the terminal acetylene is readily purified,[16] or, if the mixture is used directly in chain-extension operations, the allene is easily eliminated. Wotiz refers to the phenomenon as the propargylic rearrangement,[15] and though other explanations are possible, suggests that an intermediate ion represented as $R{\cdot}C{\equiv}C{\cdot}\overset{+}{C}H_2 \longleftrightarrow R{\cdot}\overset{+}{C}{=}C{=}CH_2$ may be involved. Thus replacement reactions with halide ions, reductive elimination of halogen, and carboxylation of propargylic Grignard reagents all lead to mixtures of the allene and acetylene.[14]

Undec-10-ynoic acid was prepared by a standard method [17] (though we obtained much higher yields than those cited without modifying the recommended procedure), and converted into dec-9-ynoic acid by Barbier–Wieland degradation.[18] Another specimen was made by carrying out the degradation on undec-10-enoic acid [18] and then brominating and dehydrohalogenating the product. As is well known,[19] terminally acetylenic alcohols



couple with formaldehyde in the presence of cuprous oxide, giving diols, and when this procedure was extended to sodium undec-9- and -10-ynoates, and the products were esterified, methyl (and ethyl) 11-hydroxyundec-9-ynoate and methyl 12-hydroxydodec-10-ynoate (XIV; R = Me) were obtained. Conversions were far from complete in the former case. In one experiment with methyl undec-10-ynoate, a low-boiling fraction was isolated which was not unchanged methyl undec-10-ynoate, but methyl undec-10-enoate. The latter was fully characterised and must arise by hydrogen transfer. On the other hand, the low-boiling fraction from the experiment with potassium dec-9-ynoate is almost entirely methyl dec-9-ynoate. The hydroxy-esters were converted into bromides, which showed no allenic bands, with phosphorus tribromide and pyridine.

[14] *Inter al.*, Wotiz, *J. Amer. Chem. Soc.*, 1950, **72**, 1639; Wotiz and Palchak, *ibid.*, 1951, **73**, 1971; Wotiz and Matthews, *ibid.*, 1952, **74**, 2559; see Jacobs and Brill, *ibid.*, 1953, **75**, 1314 for early references.
[15] Wotiz, *J. Amer. Chem. Soc.*, 1951, **73**, 693.
[16] Celmer and Solomons, *ibid.*, 1953, **75**, 3430.
[17] *Org. Synth.*, 1952, **32**, 104.
[18] Black and Weedon, *J.*, 1953, 1785.
[19] Heilbron, Jones, and Sondheimer, *J.*, 1947, 1586; Paul and Tchelitcheff, *Compt. rend.*, 1950, **230**, 1872; Heuberger and Owen, *J.*, 1952, 910.

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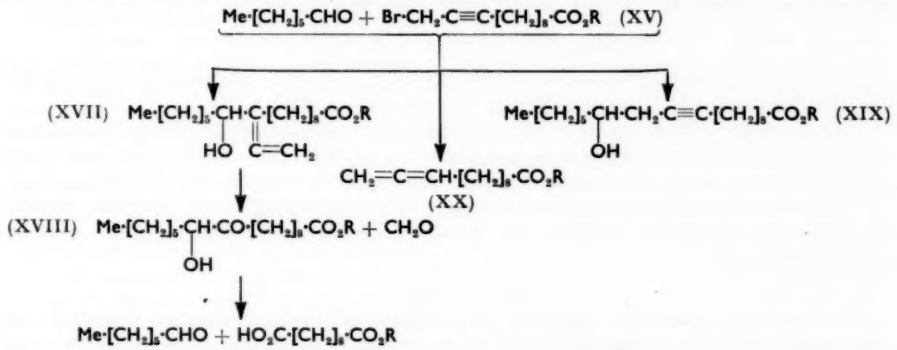
When methyl 12-bromododec-10-ynoate (XV) was treated under Reformatski conditions with heptaldehyde, and then distilled and hydrolysed, a mixture, m. p. 47—55°, of two crystalline acids was isolated. They could not be separated by fractional crystallisation from light petroleum, and reversed-phase partition chromatography did not resolve



the mixture fully. Formation of the urea clathrate compound gave a complete separation as only one acid gave a complex. The other, m. p. 61°, showed strong allenic infrared absorption (1957 cm.$^{-1}$, ε 55·7, in CCl_4), gave correct analyses for the acid (XVII; R = H), and absorbed 2 mols. of hydrogen over a catalyst. When it was ozonised under controlled conditions, and the formaldehyde produced determined quantitatively by a technique similar to that of Knights and Waight,[20] exactly one mol. was found to be released. A preparative ozonolysis experiment gave a good yield of a ketol acid which must be (XVIII), as degradation with lead tetra-acetate gave heptaldehyde and sebacic acid. Spectroscopic results are in complete agreement. The acid, m. p. 52—53°, which formed a urea complex, and is therefore less heavily branched than the other, was isomeric with it. It must be the expected homoricinstearolic acid (XIX) for, although absorbing two mols. of hydrogen over a catalyst, it showed no high-intensity ultraviolet absorption and showed no allenic vibration in the infrared spectrum. Hydroxyl and carboxyl functions were present, but, as has previously been observed for compounds of this type, the acetylenic stretching vibration is too weak to be detected [21] (cf. ricinstearolic acid). The amounts of (XVII) and (XIX) in the product were found, by intensity measurements at 1957 cm.$^{-1}$, to be 69·5% and 30·5% respectively.

When an excess of methyl 12-bromododec-10-ynoate was used in the Reformatski reaction, a new lower-boiling ester was isolated. This gave correct analyses for an ester (XX; R = Me) and had strong allenic infrared absorption though it may not be homogeneous. Dehalogenation of propargylic halides, generally secondary or tertiary, with a zinc–copper couple or lithium aluminium hydride has been used to prepare allenes though most of the examples are simple ones.[22] Hydrolysis of the ester gave a crystalline acid which was hydrogenated to dodecanoic acid. However, although its infrared spectrum showed allenic absorption at 1957 cm.$^{-1}$, the latter was very weak and further degradative work is needed to establish the structure with certainty since isomerisation of a terminal allene to the methylacetylene could occur under alkaline conditions.

Less success was attained in Reformatski experiments with methyl 12-bromoundec-9-ynoate and heptaldehyde. The products from two experiments were, after hydrolysis,

[20] Knights and Waight, *J.*, 1955, 2830; Naves, *Helv. Chim. Acta*, 1949, **32**, 1151; Doeuvre, *Bull. Soc. chim. France*, 1936, **3**, 613; cf. Naves, *ibid.*, 1956, 297.

[21] Wotiz and Miller, *J. Amer. Chem. Soc.*, 1949, **71**, 3441; Sammul, Hollingsworth, and Wotiz, *ibid.*, 1953, **75**, 4856.

[22] Bertrand, *Bull. Soc. chim. France*, 1956, 461; Ginzburg, *J. Gen. Chem.* (*U.S.S.R.*), 1940, **10**, 513, 516; Hennion and Sheehan, *J. Amer. Chem. Soc.*, 1949, **71**, 1964; Jacobs, Teach, and Weiss, *ibid.*, 1955, **77**, 6254; see also refs. 14 and 15.

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oils which could not be satisfactorily purified. A third experiment, with ethyl 12-bromoundec-9-ynoate, gave an oil which yielded to low-temperature crystallisation. The product failed to give a urea complex and was purified by crystallisation to m. p. 52—52·5°. The infrared spectrum was similar to that of the allene (XVII) : it had a strong allene band at 1955 cm.$^{-1}$ (ε 54·8, in CCl_4) and must, by analogy, be

$$Me\cdot[CH_2]_5\cdot CH(OH)\cdot C(=C=CH_2)\cdot[CH_2]_7\cdot CO_2H$$

Analytical and microhydrogenation results are in agreement. Ricinstearolic acid is undoubtedly present in the mother-liquors but was not isolated.

We conclude that in propargylic Reformatski reactions the steps involving introduction of the central functional groupings and the $\cdot[CH_2]_7\cdot CO_2H$ unit are best separated when straight-chain acids are wanted, but Reformatski reactions with $Br\cdot CH_2\cdot C{\equiv}C\cdot[CH_2]_n\cdot CO_2R$ are suited to the preparation of long-chain acids with an allenic side unit. For the synthesis of elaeostearic acid we have therefore developed further the techniques used in the synthesis of ximenynic acid.

Experimental

The ultraviolet absorption data were determined in pure ethanol with a Unicam S.P. 500 instrument. Infrared measurements were made by Mr. R. L. Erskine, B.Sc., A.R.C.S., using a Grubb-Parsons double-beam instrument. Extinction data were determined at a slit width of 0·11 mm. Analyses were carried out in the Microanalytical Laboratory (Miss J. Cuckney) of Imperial College.

Dec-3-en-1-yne (III).—Toluene-*p*-sulphonyl chloride (8·4 g.) was dissolved in warm pyridine (4 ml.) and rapidly cooled in ice to afford small crystals. Dec-1-yn-4-ol (6·2 g., containing allene, see Part II) was added slowly, and with shaking, and the mixture set aside (12 hr.). Water was added and the heavy oil removed with ether. The ethereal extracts were washed with 2N-sulphuric acid, sodium hydrogen carbonate solution, and water. After drying (Na_2SO_4) and evaporation, the crude toluene-*p*-sulphonate (II) was used without further purification. The toluene-*p*-sulphonate was dissolved in butan-1-ol, added to a solution of sodium *n*-butoxide prepared from sodium (1·0 g.) and butan-1-ol (45 ml.), at 60°, and set aside for 30 min. Water and light petroleum (b. p. 40—60°) were added, and the light petroleum layer was separated, washed with water, dried, and evaporated. Distillation gave *dec-3-en-1-yne* (2·69 g., 49%), b. p. 65°/10 mm., n_D^{20} 1·4500 (Found : C, 87·85; H, 11·85. $C_{10}H_{16}$ requires C, 88·15; H, 11·85%). Microhydrogenation, 2·8H_2. Light absorption : max. 222 mμ (ε 10,200).

The toluene-*p*-sulphonate prepared from dec-1-yn-4-ol (3·11 g.), as above, was treated at 100° in nitrogen with potassium hydroxide (1·5 g.) in water (4·5 ml.) containing two drops of detergent. After the usual working up, no product was obtained which distilled at a bath-temp. below 145°/10 mm.

Dec-1-yn-4-ol (28·1 g.), toluene-*p*-sulphonyl chloride (34·9 g.), and pyridine (14·4 g.) were allowed to react as above, and were set aside for 30 min. at 0° and 48 hr. at 20°. Working up gave the crude ester as a red oil (52·0 g., 93%). The latter was added in ether dropwise to a suspension of sodamide [from sodium (7·7 g.)] in liquid ammonia (500 ml.) and stirred overnight. Ammonium chloride (30 g.) was added, followed by water (100 ml.) and pentane (100 ml.). The pentane layer was separated and the aqueous layer further extracted with pentane (2 × 50 ml.) : the united pentane extracts were washed with water, 2N-hydrochloric acid, and sodium hydrogen carbonate solution. After drying ($MgSO_4$), the pentane was distilled through a 12" Dufton column. Distillation of the residue gave dec-3-en-1-yne (18·0 g., 79%), b. p. 70—74°/15 mm., n_D^{25} 1·4492.

16-Chlorohexadec-7-en-9-yne.—Dec-3-en-1-yne (3·32 g.) was added to sodamide [from sodium (0·62 g.)] in liquid ammonia (80 ml.). After stirring (3 hr.), 1-chloro-6-iodohexane (6·5 g.) was added and the mixture stirred overnight. Working up in the usual way gave, on distillation, *1-chlorohexadec-9-en-7-yne* (1·66 g.), b. p. 108—113°, n_D^{20} 1·4809 (Found : Cl, 14·8. $C_{16}H_{27}Cl$ requires Cl, 13·9%). Ultraviolet max. : 226 mμ (ε 10,700).

Reaction between 16-Iodohexadec-7-en-9-yne and Malonic Ester.—16-Chlorohexadec-7-en-9-yne (1·6 g.) was heated in nitrogen and under reflux, with excess of sodium iodide in acetone for 4 hr. Water was added and the solution thoroughly extracted with ether. The extracts were dried and evaporated and the residual iodo-compound, in ethanol (10 ml.), added to sodiomalonic

ester prepared from diethyl malonate (1·2 g.), sodium (0·19 g.), and ethanol (15 ml.). The mixture was heated under reflux (nitrogen) for 21 hr., then cooled, and potassium hydroxide (1·5 g.) in 95% methanol (10 ml.) was added. After 44 hr. at 20°, the crude malonic acid was isolated in the usual way and heated to 150°/10^{-6} mm. An oil (91 mg.) distilled, but it showed no light absorption characteristic of an enyne acid.

17-*Chloroheptadec-7-en-9-yne* (IV).—Sodamide was prepared by dissolving sodium (0·848 g.) in redistilled liquid ammonia. Dec-3-en-1-yne (4·45 g.) in dry ether was added and the mixture stirred for 3½ hr. with protection from moist air. 1-Chloro-7-iodoheptane (8·7 g.) was added and stirring continued overnight. Ammonium chloride (10 g.) was added and the ammonia allowed to evaporate. The residue was extracted with ether, and the extract washed, dried, evaporated and distilled, to give 17-*chloroheptadec-7-en-9-yne* (5·7 g., 65%), b. p. 100—104°/10^{-4} mm., n_D^{25} 1·4790 (Found : C, 75·35; H, 11·0; Cl, 13·0. $C_{17}H_{29}Cl$ requires C, 75·95; H, 10·85; Cl, 13·2%). Ultraviolet max. : 227 mμ (ε 14,000). The infrared spectrum (liquid film) showed bands at 2224 w (•C≡C•) and 954 cm.$^{-1}$ (*trans*-CH=CH conjugated with an acetylenic linkage).

Octadec-trans-11-*en*-9-*ynoic* (*Ximenynic*) *Acid* (VII).—17-Chloroheptadec-7-en-9-yne (2·5 g.), sodium iodide (1·0 g.), and sodium cyanide (1·0 g.) in 80% ethanol (12 ml.) were heated under reflux (40 hr.) in nitrogen. Potassium hydroxide (5·0 g.) in water (12 ml.) was added, and refluxing continued until no more ammonia was liberated (29 hr.). The acidic product was isolated in the usual way and dissolved in hot methanol (50 ml.), containing urea (15 g.). On cooling to 0°, a clathrate compound crystallised which was washed with a little ice-cold methanol saturated with urea and then decomposed by dilute hydrochloric acid. The solid product (0·87 g.) had m. p. 35—37°. By dilution with water and ether-extraction, the methanolic filtrate from the complex gave crude acid which, after crystallisation from 80% methanol, melted over several degrees up to 30° (0·21 g.).

Crude ximenynic acid, m. p. 35—37°, was recrystallised from light petroleum (b. p. 40—60°) and the acid formed white plates, m. p. and mixed m. p. 39—40° (Found : C, 77·35; H, 10·9. Calc. for $C_{18}H_{30}O_2$: C, 77·65; H, 10·85%). Microhydrogenation : 2·95H_2. Ultraviolet max. 228 mμ (ε 16,800). Infrared bands at 2224 (C≡C), 952 (*trans*-C=C), and 1708 cm.$^{-1}$ (CO_2H). On hydrogenation and crystallisation from 80% ethanol, stearic acid, m. p. and mixed m. p. 70°, was obtained. Recorded data [4] for natural ximenynic acid are m. p. 39—40°, $\lambda_{max.}$ 229 mμ (ε 16,600). The infrared bands of the natural acid include those just listed.

4-2′-*Tetrahydropyranyloxypent*-1-*yne* (X).—Tetrahydrofurfuryl chloride, prepared [23] in 67% yield, had b. p. 46°/13 mm., n_D^{22} 1·4540—1·4544. It was converted into pent-4-yn-1-ol by the sodamide ring-fission method of Eglinton, Jones, and Whiting.[11] Pent-4-yn-1-ol (72% yield) had b. p. 59°/8 mm., n_D^{24} 1·4430—1·4437, and was converted into the tetrahydropyranyl ether, b. p. 90—94°/10 mm., n_D^{22} 1·4561—1·4565, in the usual way (95% yield).

7-2′-*Tetrahydropyranyloxyhept*-3-*yn*-1-*ol* (XI).—4-2′-Tetrahydropyranyloxypent-1-yne (117·6 g.) in ether (120 ml.) was added to sodamide prepared from sodium (16·8 g.) in liquid ammonia (3·5 l.). After 3½ hours' stirring ethylene oxide (40 ml.) in dry ether (100 ml.) was added, and the mixture stirred for 19 hr. The ammonia was allowed to evaporate, water (1 l.) added, and the product extracted three times with ether (total, 1½ l.). The extracts were dried ($MgSO_4$), evaporated, and distilled. A fraction (48 g., 41%), b. p. 90—120°/13 mm., n_D^{21} 1·4558—1·4570, was largely unchanged 4-2′-tetrahydropyranyloxypent-1-yne and was followed by 7-2′-*tetrahydropyranyloxyhept*-3-*yn*-1-*ol* which distilled as a viscous oil (73·0 g., 82% yield, 50% discounting recovered material), b. p. 143—158°/0·1 mm., n_D^{21} 1·4798—1·4805 (Found : C, 67·9; H, 9·6. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%).

In a second experiment, pent-4-yn-1-ol (176 g.) was mixed with dihydropyran (183 g.) and a few drops of phosphorus oxychloride in the usual way, and after 2 hr. added to a solution of sodamide (from sodium, 50·5 g.) in liquid ammonia (6 l.) as above. The amount of ethylene oxide was increased to provide a 50% excess. This resulted in a yield of 82% (271 g.) and an increased conversion (61%).

Hept-3-*yne*-1 : 7-*diol*.—7-2′-Tetrahydropyranyloxyhept-3-yn-1-ol (71·5 g.) was refluxed in methanol (620 ml.) with toluene-*p*-sulphonic acid (1·2 g.) for 1¼ hr. Sodium carbonate (0·8 g.) was added, and most of the methanol evaporated. After filtration, distillation of the filtrate gave hept-3-yne-1 : 7-diol (39·1 g., 90%), b. p. 111—124°/0·1 mm., n_D^{22} 1·4837—1·4840 (Found : C, 65·55; H, 9·55. Calc. for $C_7H_{12}O_2$: C, 65·6; H, 9·45%). Jones, Mansfield, and Whiting [24]

[23] *Org. Synth.*, 1945, **25**, 84.
[24] Jones, Mansfield, and Whiting, *J.*, 1954, 3208.

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give b. p. 102—104°/0·05 mm., n_D^{18} 1·4870, for a specimen made by a similar procedure but *via* a Grignard intermediate.

Heptane-1 : 7-*diol*.—Hept-3-yne-1 : 7-diol (30·5 g.) in methanol (250 ml.) was completely hydrogenated over Raney nickel at 20°/30—50 atm. The catalyst was filtered off, the methanol evaporated, and the residue distilled. Heptane-1 : 7-diol (28·8 g., 91%) was obtained having b. p. 117—126°/0·03 mm., n_D^{24} 1·4527—1·4540, m. p. 20° (Found : C, 63·85; H, 12·15. Calc. for $C_7H_{16}O_2$: C, 63·6; H, 12·2%). Huber [10] gives b. p. 112—115°/3 mm., n_D^{25} 1·4520, m. p. 20—22°.

On a larger scale, undistilled 7-2′-tetrahydropyranyloxyhept-3-yn-1-ol (271 g.) was refluxed in methanol (1800 ml.) containing toluene-*p*-sulphonic acid (3 g.) for 2 hr. Potassium hydroxide (1·0 g.) was then added and the solution evaporated to 500 ml. Raney nickel was added and the mixture hydrogenated at 20°/130 atm. Working up as above gave heptane-1 : 7-diol (170·7 g., 100%).

Hept-3-yne-1 : 7-diol (36·1 g.) was hydrogenated in methanol (100 ml.) over 5% palladium–barium sulphate (absorption, 12·45 l. at N.T.P. Theor., 12·63 l.). The catalyst was removed, the solvent evaporated, and the residual oil distilled, to give *n*-heptanol (4·55 g.), b. p. 40—42°/0·2 mm., n_D^{18} 1·4248. The α-naphthylurethane crystallised from light petroleum (b. p. 100—120°) in plates, m. p. 56°, undepressed when admixed with an authentic specimen m. p. 57° (Found : C, 75·45; H, 8·0. Calc. for $C_{18}H_{23}O_2N$: C, 75·75; H, 8·1%). Continued distillation gave heptane-1 : 7-diol (3·3 g.), b. p. 107—108°/0·1 mm., n_D^{22} 1·4521, m. p. 16—18°. A large white spongy residue remained in the flask.

1 : 7-*Dichloroheptane*.—Heptane-1 : 7-diol (170 g.) was mixed with pyridine (22 ml.), and thionyl chloride (660 g.) added dropwise with stirring, at 0°. The product was heated on the steam-bath for 2 hr., cooled, poured into ice, and extracted with light petroleum (b. p. 40—60°) (3 × 500 ml.). The extract was washed twice with concentrated sulphuric acid (150 ml.), twice with saturated sodium hydrogen carbonate solution, and finally with water. Drying (Na_2SO_4), evaporation, and distillation gave 1 : 7-dichloroheptane (147 g., 69%), b. p. 106—110°/15 mm., n_D^{19} 1·4591. The yield is low because of an accidental loss. Huber gives b. p. 124—125°/35 mm., n_D^{25} 1·4565.

1-*Chloro*-7-*iodoheptane*.—1 : 7-Dichloroheptane (147 g.) was heated under reflux with sodium iodide (125 g.) in acetone (1 l.) for 4 hr. Most of the acetone was distilled off and water and ether added. The ether extracts were washed with sodium thiosulphate solution, and then water, dried, evaporated, and distilled through a Dufton column. Material of b. p. 52—56°/0·5 mm., n_D^{20} 1·4609, was recovered dichloroheptane (64·5 g., 44%). Chloroiodoheptane, b. p. 82—84°/0·5 mm., n_D^{23} 1·5136, was then isolated in 40% yield (91 g.). Huber [10] gives b. p. 95°/2 mm., n_D^{25} 1·5158.

Undec-10-*ynoic Acid*.—This was prepared from undecenoic acid (157·5 g.) according to the directions given in *Org. Synth.*[17] Undec-10-ynoic acid, b. p. 134°/0·06 mm., m. p. 41—43°, was obtained. One crystallisation raised the m. p. to 42·5° (125 g., 79%) (lit.,[17] m. p. 42·5—43°; 38—49% yield). One further crystallisation from light petroleum (b. p. 40—60°) raised the m. p. to 43—43·5°. The above yield was reproduced in other runs. The methyl ester, prepared by esterification with methanolic sulphuric acid, had b. p. 78°/0·04 mm., n_D^{21} 1·4452 (92%).

Methyl 12-*Hydroxydodec*-10-*ynoate* (XIV; R = Me).—Undec-10-ynoic acid (97 g.) was neutralised with aqueous sodium hydroxide solution (~500 ml.), and cuprous oxide [prepared from cuprous chloride (70 g.) by dissolution in 5N-hydrochloric acid and precipitation with 40% potassium hydroxide solution] added, together with 40% aqueous formaldehyde (500 ml.) and calcium carbonate (4 g.). The mixture was heated and stirred under nitrogen on a steam-bath for 40 hr., and then acidified with 2N-hydrochloric acid and extracted with ether. The extracts were washed with 3N-hydrochloric acid until the washings were no longer coloured, dried, and evaporated. Methanol (200 ml.), benzene (300 ml.), and sulphuric acid (40 ml.) were added to the residue and the mixture heated under reflux in nitrogen for 10 hr. The ester was isolated in the usual way and on distillation *methyl* 12-*hydroxydodec*-10-*ynoate* (40·0 g., 33%), b. p. 162—172°/0·3 mm., n_D^{21} 1·4656, was obtained (Found : C, 68·35; H, 9·9. $C_{13}H_{22}O_3$ requires C, 68·95; H, 9·8%). The infrared spectrum showed maxima at 3413 s (OH), 2291 mw and 2234 mw (·C≡C·) and 1734 s cm.$^{-1}$ (ester). The hydroxy-ester crystallised at 0° in long white needles, m. p. 20°, but was not recrystallised. The 1-*naphthylurethane* crystallised as plates from light petroleum (b. p. 100—120°), m. p. 63—63·5° (Found : C, 72·6; H, 7·5; N, 3·6. $C_{24}H_{29}O_4N$ requires C, 72·9; H, 7·4; N, 3·55%). A low-boiling fraction, b. p. 80°/0·1 mm.

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(20·2 g.), was also isolated in the above distillation and, as it gave a precipitate with alcoholic silver nitrate, it contains at least some recovered methyl undec-10-ynoate.

In another experiment methyl undec-10-ynoate (8·1 g.) was heated and stirred for 45 hr. with 40% formaldehyde solution (20 ml.) in dioxan (35 ml.) and cuprous oxide (from 4·5 g. of cuprous chloride). After working up as before, methyl 12-hydroxydodec-10-ynoate (2·1 g.), b. p. 131—136°/0·03 mm., n_D^{24} 1·4661, was obtained, together with a fraction, b. p. 66°/0·04 mm., n_D^{23} 1·4379 (1·43 g.). The latter gave no precipitate with alcoholic silver nitrate and analysed correctly for methyl undec-10-enoate (Found: C, 72·65; H, 11·25. Calc. for $C_{12}H_{22}O_2$: C, 72·7; H, 11·2%). Microhydrogenation 1·0H_2. On hydrolysis (0·65 g. of ester), undec-10-enoic acid (0·44 g.), m. p. 22°, was obtained, which gave a *p*-bromophenacyl ester, m. p. 60°. Mixed m. p.s with authentic specimens were undepressed.

12-*Hydroxydodec*-10-*ynoic Acid* (XIV; R = H).—Hydrolysis of the methyl ester (0·50 g.) with ethanolic potassium hydroxide, and recrystallisation of the acidic product from 1 : 1 acetone–light petroleum (b. p. 60—80°), gave 12-*hydroxydodec*-10-*ynoic acid* (0·32 g.), m. p. 73° (Found: C, 67·8; H, 9·6. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%). The *p*-bromophenacyl ester crystallised from ethanol in plates, m. p. 63·5°.

Methyl 12-*Bromododec*-10-*ynoate* (XV; R = Me).—Methyl 12-hydroxydodec-10-ynoate (7·29 g.), dissolved in dry ether (12 ml.) and pyridine (0·5 ml.), was cooled in ice and stirred whilst phosphorus tribromide (3·22 g.) was added dropwise. The mixture was stirred for 1 hr. at 0° and for 30 min. at 20°. Ether and ice-cold 2N-hydrochloric acid were added and the ether layer was separated, washed with 2N-hydrochloric acid and water, and dried ($MgSO_4$). The ether was evaporated under reduced pressure and the *methyl* 12-*bromododec*-10-*ynoate* distilled; it had b. p. 136°/10^{-3} mm., n_D^{23} 1·4860 (Found: C, 54·25; H, 7·45; Br, 27·5. $C_{13}H_{21}O_2Br$ requires C, 54·0; H, 7·3; Br, 27·65%). The yield was 5·64 g. (61%). The infrared spectrum (liquid film) showed an acetylenic linkage (2309 w and 2239 m cm.$^{-1}$) but no allenic absorption.

Reformatski Reaction between Methyl 12-*Bromododec*-10-*ynoate and Heptaldehyde*.—Zinc (1·2 g.; washed with 2N-hydrochloric acid and then dried) was treated with some of a mixture of methyl 12-bromododec-10-ynoate (5·01 g.), heptaldehyde (2·31 g.), and dry tetrahydrofuran (20 ml.). Mercuric chloride (50 mg.) was added and, after a few minutes on the steam-bath, reaction began and the solution became pale green. The remainder of the reactants was then added dropwise and, finally, the product was heated under reflux (45 min.) and set aside overnight. A little zinc (0·17 g.) remained unused. Iced dilute acetic acid was added and the product extracted well with ether. The ether extracts were united, washed with sodium hydrogen carbonate solution and then with water, dried ($MgSO_4$), evaporated, and distilled. The distillate (2·03 g., 36%), b. p. 152—174°/3 × 10^{-4} mm., $n_D^{19\cdot5}$ 1·4702—1·4711, was hydrolysed for 2 hr., under reflux, with potassium hydroxide (0·60 g.) in ethanol (15 ml.) and water (1 ml.). Water was added, the potassium salts were extracted with ether, and the extracts rejected. The aqueous layer was acidified and then extracted with ether, and the ether extracts were dried and evaporated. Crystallisation of the residue (twice) from light petroleum (b. p. 60—80°) gave white plates, m. p. 47—53° (0·81 g.) (Found: C, 72·9; H, 11·05. Calc. for $C_{19}H_{34}O_3$: C, 73·45; H, 11·05%). The mixture of acids showed no high-intensity maximum in the ultraviolet and in the infrared spectrum (paraffin mull) bands were present at 3300 s and 3195 s (OH), 1957 m (allene) and 1711 s cm.$^{-1}$ (CO_2H).

Methyl 12-bromododec-10-ynoate (6·59 g.), heptaldehyde (1·9 g.; for complete reaction with the bromo-compound 2·6 g. are needed), and zinc (1·45 g.) gave, on Reformatski reaction, the mixed ester (1·50 g.) mentioned above, together with an *ester*, b. p. 86—96°/0·05 mm., $n_D^{21\cdot5}$ 1·4550. (Found: C, 74·3; H, 10·8. $C_{13}H_{22}O_2$ requires C, 74·25; H, 10·55%). The latter had a medium-strong infrared band (liquid film) at 1957 cm.$^{-1}$, indicating an allenic function (ester 1731 s cm.$^{-1}$). By alkaline hydrolysis an *acid* was obtained, having, after crystallisations, m. p. 45—46° (Found: C, 72·8; H, 10·35. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·25%). The p-*bromophenacyl ester* crystallised in plates (from ethanol), m. p. 56—57° (Found: C, 60·65; H, 6·3. $C_{20}H_{25}O_3Br$ requires C, 61·05; H, 6·4%). On hydrogenation the acid gave lauric acid (m. p. and mixed m. p. 43—44°). As the allene absorption (in CCl_4 solution) at 1957 cm.$^{-1}$ was much weaker than that of the original ester, acceptance of its structure as dodec-10 : 11-dienoic acid requires further degradative evidence.

13-*Hydroxynonadec*-10-*ynoic* (*homoricinstearolic*) (XIX) *and* 11-*Hydroxy*-10-*vinylideneheptadecanoic Acid* (XVII). The Reformatski product, m. p. 47—53° (473 mg., see above), was dissolved in methanol (10 ml.) containing urea (2 g.). Cooling in ice gave a clathrate compound

which was removed. After recrystallisation from methanol (5 ml.) saturated with urea, water was added and 13-*hydroxynonadec*-10-*ynoic acid* (85 mg.) filtered off. It had m. p. 48—51°, raised by crystallisation from light petroleum (b. p. 60—80°) to m. p. 52—53° (white plates) (Found : C, 73·5; H, 11·1. $C_{19}H_{34}O_3$ requires C, 73·45; H, 11·05%). Microhydrogenation 1·96H_2. No allenic or acetylenic absorption was present in the infrared spectrum (paraffin mull). There were bands at 3330 m and 1081 m (OH) and 1712 s and 1694 s cm.$^{-1}$ (CO_2H doublet).

The methanolic filtrate from urea clathrate formation was treated further with urea (2 g.), and the crystals, which were deposited on cooling, were filtered off. On decomposition with water only a slight turbidity was formed. Water was added to the filtrate and 11-*hydroxy*-10-*vinylideneheptadecanoic acid* (301 mg.) filtered off. It had m. p. 57—59° raised by two recrystallisations from light petroleum (b. p. 60—80°) to 61° (Found : C, 73·6; H, 11·2%). Microhydrogenation 2·0H_2. The allenic band at 1957 cm.$^{-1}$ had ε 55·7 in CCl_4. The mixture, m. p. 47—53°, had ε 38·8 at 1957 cm.$^{-1}$ and thus contains 69·5% of 11-hydroxy-10-vinylideneheptadecanoic acid.

Ozonolysis of 11-*Hydroxy*-10-*vinylideneheptadecanoic Acid*.—The acid (56·0 mg.) was dissolved in purified acetic acid–ethyl acetate (5 ml.) in a 15 ml. bubbler attached to the ozoniser. A second bubbler contained further solvent (2 ml.). Ozonised oxygen was passed through the two bubblers and then into a 20 ml. portion of 2% potassium iodide which was renewed and titrated at 1 min. intervals. After 15 min., when successive titration figures had become constant, the solutions were washed into a 250 ml. graduated flask, and a standard Schiff's reagent (75 ml.) added, followed by concentrated hydrochloric acid (37·5 ml.) and water to adjust the volume. The solution was set aside for 3 hr. at 22° and the absorption at 570 mμ measured with a Unicam SP 600 instrument. The reading was compared with a calibration curve and, after correction for a small solvent blank (0·12 mg.), corresponded to 5·42 mg. (100%) of formaldehyde. Standard Schiff's reagent was prepared by dissolving rosaniline hydrochloride (1 g.) in distilled water (500 ml.), and adding a solution of sodium sulphite (25 g.) in water (460 ml.) and then concentrated hydrochloric acid (15 ml.). The solution was set aside overnight and then decolorised with charcoal. Standard formaldehyde solutions for calibration (*ca.* 0·4%) were estimated by oxidation with hydrogen peroxide in the presence of 0·1N-alkali followed by back-titration with 0·1N-hydrochloric acid to thymol-blue.

11-*Hydroxy*-10-*oxoheptadecanoic Acid* (XVIII).—11-Hydroxy-10-vinylideneheptadecanoic acid (84 mg.) was ozonised in ethyl acetate (3 ml.) and glacial acetic acid (2 ml.) at 0° for 20 min. The solvent was partly evaporated under reduced pressure and water added. 11-*Hydroxy*-10-*oxoheptadecanoic acid* (58 mg.) was filtered off; it had m. p. 67·5—68·5°, raised by recrystallisation to 68·5° (Found : C, 68·35; H, 10·55. $C_{17}H_{32}O_4$ requires C, 67·95; H, 10·75%). The infrared spectrum (paraffin mull) showed bands at 3279 s and 3185 s cm.$^{-1}$ (OH), 1711 s cm.$^{-1}$ (CO_2H), and 1682 s cm.$^{-1}$ (bonded CO). There was no allene absorption.

Action of Lead Tetra-acetate on 11-*Hydroxy*-10-*oxoheptadecanoic Acid*.—Lead tetra-acetate (57·8 mg.) and 11-hydroxy-10-oxoheptadecanoic acid (24·2 mg.) were dissolved in 90% acetic acid (1 ml.) and set aside for 1 hr. : the odour of heptaldehyde could be detected. Concentrated sulphuric acid (18 mg.) was added and the lead sulphate centrifuged off. After being made just alkaline, the solution was extracted with ether, and the ether extracts were added to methanolic 2 : 4-dinitrophenylhydrazine hydrochloride and set aside for 1 hr. The product was evaporated on a steam-bath and the residue chromatographed on alumina with benzene–ether (2 : 1) as eluant. The fast-running band was isolated and gave crude *n*-heptaldehyde 2 : 4-dinitrophenylhydrazone (9·6 mg.), m. p. 102°. When recrystallised from 90% methanol it had m. p. 104° (3·4 mg.), undepressed by an authentic specimen (m. p. 106°).

The aqueous layer after removal of heptaldehyde was acidified, washed with light petroleum (b. p. 60—80°), and evaporated to dryness. Sebacic acid (6·1 mg.), isolated from the residue by ether-extraction followed by recrystallisation from water, had m. p. 132—133°. The mixed m. p. with an authentic specimen, m. p. 133—134°, was 133°.

1 : 1-*Diphenylundec*-1-*en*-10-*yne*.—Phenylmagnesium bromide was prepared from bromobenzene (390 g.), magnesium (60 g.), and ether. Ethyl undec-10-ynoate (160·5 g., prepared [25] in 92% yield) was dissolved in ether and added during 4 hr. to the stirred Grignard reagent. Next morning, ice-cold dilute sulphuric acid and ether were added. The ether extracts were dried ($MgSO_4$) and the ether was evaporated. The yellow oily residue was dehydrated in an oil-bath at 220—230° (1 hr.) and then distilled, to give 1 : 1-diphenylundec-1-en-10-yne (211 g.,

[25] Jeffrey and Vogel, *J.*, 1948, 674.

92%), b. p. 174—180°/0·2 mm., n_D^{24} 1·5578—1·5599, which crystallised in a few minutes (m. p. 34°; plates). Ultraviolet max: 251 mμ (ε 18,100). Black and Weedon [18] report b. p. 152°/0·02 mm., n_D^{21} 1·5620, $\lambda_{max.}$ 251 mμ (ε 18,000) (70% yield), but no m. p.

Dec-9-ynoic Acid.—(*a*) 1 : 1-Diphenylundec-1-en-10-yne (210 g.) was dissolved in glacial acetic acid (2 l.) and stirred whilst chromium trioxide (143 g.) in water (250 ml.) was added dropwise at 55—60°. Procedure according to Black and Weedon's directions [18] gave dec-9-ynoic acid (70 g., 60%), b. p. 123—126°/0·03 mm., n_D^{21} 1·4560, m. p. 22°. Lit.,[18] b. p. 88°/0·1 mm., n_D^{27} 1·4565, m. p. 22°.

(*b*) By chromic oxide oxidation,[18] 1 : 1-diphenylundeca-1 : 10-diene gave dec-9-enoic acid (63%), b. p. 124—126°/0·05 mm., n_D^{23} 1·4480. Dec-9-enoic acid (51·9 g.) in ether (300 ml.) was treated with bromine (approx. 15 ml.) until a slight excess remained. The crude dibromide was added to sodamide in liquid ammonia (1·5 l.) prepared from sodium (32·4 g.), and the mixture was stirred overnight. Ammonium chloride (50 g.) was added and the ammonia allowed to evaporate. Working up in the usual way gave dec-9-ynoic acid (40·8 g., 80%), b. p. 110—118°/10^{-4} mm., n_D^{21} 1·4592, m. p. 19—22·5° (five fractions).

1 : 1-*Diphenylundeca*-1 : 10-*diene*.—Prepared according to Black and Weedon's directions and dehydrated at 230° for 45 min. this had b. p. 186—188°/0·3 mm., n_D^{22} 1·5550 (yield 148 g., 70%). Lit.,[18] b. p. 228—230°/12—14 mm., n_D^{21} 1·5545 (yield 80%).

Methyl 11-*Hydroxyundec*-9-*ynoate*.—Dec-9-ynoic acid (57·2 g.) was neutralised with potassium hydroxide in ethanol (150 ml.); cuprous oxide (from 50 g. of cuprous chloride), 40% aqueous formaldehyde (360 ml.), and calcium carbonate (5 g.) were added. Procedure as described for methyl 12-hydroxydodec-10-ynoate gave (i) recovered methyl dec-9-ynoate (30·5 g.), b. p. 70—76°/10^{-4} mm., n_D^{23} 1·4433, infrared bands (liquid film) at 3257 m and 2126 w cm.$^{-1}$ (C≡CH) and 1736 s cm.$^{-1}$ (CO_2Me), which was hydrolysed to dec-9-ynoic acid, m. p. 18—20°, n_D^{25} 1·4563, and (ii) *methyl* 11-*hydroxyundec*-9-*ynoate* (11·0 g.), b. p. 123—124°/0·002 mm., n_D^{23} 1·4646 (Found: C, 67·65; H, 9·65. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%). The latter ester had infrared bands (liquid film) at 3413 s cm.$^{-1}$ (OH), 2288 w and 2230 mw cm.$^{-1}$ (C≡C) and 1734 s cm.$^{-1}$ (CO_2Me). A similar preparation from decynoic acid (60·2 g.), esterified with ethanol, yielded ethyl dec-9-ynoate (30 g.) and ethyl 11-hydroxyundec-9-ynoate (9·63 g.), b. p. 130—131°/10^{-4} mm., n_D^{21} 1·4654.

Methyl 11-*Bromoundec*-9-*ynoate*.—Methyl 11-hydroxyundec-9-ynoate (8·17 g.) was dissolved in dry ether (15 ml.) and pyridine (0·5 ml.), cooled in ice, and phosphorus tribromide (4·00 g.) was added dropwise. The mixture was stirred at 0° for 1 hr. and at 20° for 1 hr. and worked up as was methyl 12-bromododec-10-ynoate. On distillation *methyl* 11-*bromoundec*-9-*ynoate* (6·92 g., 65%), b. p. 132—133°/2 × 10^{-4} mm., n_D^{21} 1·4910, was obtained (Found: C, 52·1; H, 7·0. $C_{12}H_{19}O_2Br$ requires C, 52·35; H, 6·95%). The corresponding ethyl ester, prepared similarly, had b. p. 117—121°/0·03 mm., n_D^{18} 1·4830.

10-*Hydroxy*-9-*vinylidenehexadecanoic Acid*.—Ethyl 12-bromoundec-9-ynoate (3·63 g.) and heptaldehyde (1·70 g.) were added gradually to zinc wool (1·1 g.), activated by mercuric chloride, in tetrahydrofuran (5 ml.). Three drops of propargyl bromide had to be added to start the reaction: the solution became green and was heated on a steam-bath overnight. Water and acetic acid were added and the solution was extracted thoroughly with ether. The ethereal extracts were washed with sodium hydrogen carbonate solution and with water, dried, evaporated and distilled at 160°/10^{-6} mm. Redistillation gave an ester (1·01 g.), b. p. 150—174°/5 × 10^{-3} mm., n_D^{21} 1·4672—1·4684, which was hydrolysed by potassium hydroxide (1·0 g.) in boiling ethanol (9 ml.) and water (1 ml.) for 75 min. On working up in the usual way an acid which crystallised reluctantly at 0° was obtained: it was almost molten at 20°. The acid crystallised from acetone at −70° as plates (0·203 g.), m. p. 48—52°. [Infrared absorption at 1955 cm.$^{-1}$, ε 54·6 (in CCl_4) indicated that it was nearly pure allene.] The *acid* failed to form a clathrate compound with urea and was crystallised twice from light petroleum (b. p. 40—60°) to m. p. 52—52·5° (Found: C, 72·7; H, 10·9. $C_{18}H_{32}O_3$ requires C, 72·9; H, 10·9%). The intensity of absorption at 1955 cm.$^{-1}$ was ε 54·8. Two attempts to repeat the isolation using the methyl ester gave oily acidic products which could not be adequately purified.

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Department of Chemistry,
Imperial College of Science and Technology,
South Kensington, London, S.W.7.

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XUM

311. *Lipids. Part VI.* Total Synthesis of α- and β-Elæostearic and Punicic (Trichosanic) Acid.*

By L. Crombie and A. G. Jacklin.

Trichosanic is shown to be identical with punicic acid. As a preliminary to synthetic work, the stereochemistry of the natural octadeca-9 : 11 : 13-trienoic acids is discussed. Octadeca-*cis*-9 : *trans*-11 : *trans*-13-trienoic acid is synthesised and is identical with natural α-elæostearic acid. The synthesis involves propargylic Reformatski reaction with hept-2-enal, followed by formal dehydration to deca-3 : 5-dien-1-yne. Chain extension with 1-chloro-7-iodoheptane and nitrile synthesis gives octadeca-*trans*-11 : *trans*-13-dien-9-ynoic acid which is stereospecifically hydrogenated. The synthetic *cis*-9 : *trans*-11 : *trans*-13-acid is stereomutated, and the all-*trans*-product is identical with β-elæostearic acid.

Similarly, hept-2-ynal is converted into dec-3-ene-1 : 5-diyne, and octadec-11-ene-9 : 13-diynoic acid built up. Stereospecific partial hydrogenation gives octadeca-*cis*-9 : *trans*-11 : *cis*-13-trienoic acid which is identical with natural punicic (trichosanic) acid (previously thought to be a *trans* : *cis* : *cis*-stereoisomer). Oxidative coupling of oct-3-en-1-yne with dec-9-ynoic acid, followed by esterification, gives octadec-13-ene-9 : 11-diynoate. Partial hydrogenation and hydrolysis gives octadeca-*cis*-9 : *cis*-11 : *trans*-13-trienoic acid which was not fully purified but differs from the natural acids. Octadeca-*trans*-9 : *trans*-11-dienoic acid is sythesised by a new variant of the Wittig reaction : this indicates an alternative route to octadeca-9 : 11 : 13-trienoic acids.

α-Elæostearic acid, m. p. 48°, is the principal fatty acid of tung oil [1,2] which is expressed from the seeds of *Aleurites fordii* and *A. montana* (family Euphorbiaceae). Other natural sources of α-elæostearic acid are known,[2] and the acid was first investigated by Cloez [3] in 1875. For some time it was thought to be octadeca-9 : 13-dienoic acid, as valeraldehyde and 8-formyloctanoic acid were produced by ozonolysis, whilst on treatment with bromine a tetrabromide was obtained.[4] The correct structure, octadeca-9 : 11 : 13-trienoic acid (X) was not appreciated until 1925 when Böeseken and Ravenswaay [5] found that the acid absorbed three mols. of hydrogen over a catalyst and had a high exaltation of molecular refractivity. Eibner and Rossman then showed that ozonolysis also gave glyoxal.[6] Formation of a hexabromide,[7] and ultraviolet absorption data,[8] support the conjugated triene structure. There are eight geometrical isomers possible for structure (X), and on treatment with iodine in the presence of ultraviolet light a second stereoisomer, β-elæostearic acid, m. p. 71°, is produced. From time to time other possible stereoisomers have been alleged to exist in Nature but some have been shown to be mixtures, and others are now known to have entirely different structures. Nevertheless, two other natural triene acids are usually accepted as stereoisomers of (X) : they are punicic and trichosanic acids.

Punicic acid, m. p. 43·5—44°, was isolated by Toyama and Tsuchiya [9] from seed oil

* Part V, preceding paper.

[1] *Inter al.*, O'Connor, Heinzelman, Freeman, and Pack, *Ind. Eng. Chem. Analyt.*, 1945, **17**, 467; Hilditch and Riley, *J. Soc. Chem. Ind.*, 1946, **65**, 74.

[2] For general information consult Eckey, "Vegetable Fats and Oils," Reinhold, New York, 1954; Hilditch, "The Chemical Constitution of Natural Fats," Chapman and Hall, London, 1956; Ralston, "Fatty Acids and their Derivatives," Wiley, New York, 1948; Markley, "Fatty Acids," Interscience Publ. Inc., New York, 1947.

[3] Cloez, *Compt. rend.*, 1875, **81**, 469; 1876, **82**, 501; 1876, **83**, 943.

[4] Maquenne, *ibid.*, 1902, **135**, 696; Kametaka, *J.*, 1903, 1042; Majima, *Ber.*, 1909, **42**, 674.

[5] Böeseken and Ravenswaay, *Rec. Trav. chim.*, 1925, **44**, 241.

[6] Eibner and Rossmann, *Chem. Umschau*, 1928, **35**, 197.

[7] Bauer and Rohrbach, *ibid.*, p. 53; van Loon, *Rec. Trav. chim.*, 1931, **50**, 32.

[8] Manecke and Volbert, *Farben Ztg.*, 1927, 2829, 2887.

[9] Toyama and Tsuchiya, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1935, **38**, 182B.

of the pomegranate, *Punica granatum* (family Punicaceae), and gives azelaic and *n*-valeric acid on ozonolysis; oxalic acid and glyoxal are also probably formed. The methyl ester gives methyl hydrogen azelate and a corresponding semialdehyde when ozonised. Punicic acid is readily isomerised to β-elæostearic acid. Trichosanic acid, m. p. 35—35·5°, was originally isolated by the same authors [10] from the seed oil of the Japanese snake-gourd or karasu-uri, *Trichosanthes cucumeroides* (family Cucurbitaceae), and shown to be isomerised to β-elæostearic acid by iodine. Lately [11] the same acid, m. p. 34—35°, has been reported in Indian snake-gourd oil (*T. anguina*). We deal first with the individuality of these acids.

α- and β-Elæostearic acid are thoroughly characterised. Punicic acid was carefully re-examined by Farmer and van den Heuvel [12] who were convinced that it was a third stereoisomer of (X): the present work is in full agreement. Punicic acid depresses the m. p. of α- and β-elæostearic acids and has different spectral characteristics. Toyama and Tsuchiya's grounds [10] for considering trichosanic acid as a fourth stereoisomer were

TABLE 1. *Ultraviolet light absorption data for octadeca-9 : 11 : 13-trienoic acids.*

	Natural			Synthetic		
Acid	M. p.	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$	M. p.	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$
β-Elæostearic * [*trans*-9 : *trans*-11 : *trans*-13]	72°	259	47·0	71°	258	42·0
		268	61·0		268	58·0
		279	49·0		279	45·5
α-Elæostearic * [*cis*-9 : *trans*-11 : *trans*-13]	48	261	36·0	47	261	35·0
		271	47·0		270	47·0
		281	38·0		281	36·5
Punicic [*cis*-9 : *trans*-11 : *cis*-13]	43·5—44	264	35·0			
		274	46·0			
		285	36·5	43—43·5	264	34·0
Japanese trichosanic [*cis*-9 : *trans*-11 : *cis*-13]	43—43·5	264	33·5		274	45·5
		274	44·5		285	34·0
		285	35·5			
Indian trichosanic [*cis*-9 : *trans*-11 : *cis*-13 +20% of satd. acids]	43	264	26·5			
		274	37·0			
		285	29·0			

* Data for these two natural acids from Crombie and Tayler.[41]

TABLE 2. *Infrared extinction data* (CS_2) *for octadeca-9 : 11 : 13-trienoic acids and related compounds.**

Acid	$\lambda_{max.}$ (cm.$^{-1}$)	ε [a]	$\varepsilon_2/\varepsilon_1$ [a]	ε [b]	$\varepsilon_2/\varepsilon_1$ [b]	$\lambda_{max.}$ [c] (cm.$^{-1}$)	ε [c]	$\varepsilon_2/\varepsilon_1$ [c]
β-Elæostearic	994	760	5·65	795	4·3	995	545	3·2
α-Elæostearic	992	365	2·7	400	2·15	992	395	2·3
	963	40	—	100	—	964	115	—
Punicic	987	160	1·2	190	1·05	988	175	1·05
	937	105	—	195	—	937	195	—
Trichosanic (Jap.) ...	987	155	—	190	—	—	—	—
	937	100	—	195	—	—	—	—
Trichosanic (Indian)	986	125	—	150	—	—	—	—
	936	80	—	170	—	—	—	—
Elaidic	965	135	1	185	1	967	170	1
Ximenynic	951	172	—	230	—	—	—	—

* Slit width 0·21 mm.: the absolute value for ε must be expected to vary according to the spectrometer used. $\varepsilon_2/\varepsilon_1$ is the ratio of ε for the sample to that of elaidic acid. All acids are of natural origin: data for synthetic acids are in the Experimental section.

[a] Background absorption eliminated by extrapolation. [b] Background absorption not eliminated. [c] Values by Ahlers *et al.* [21, 24] (calc. from their values for specific extinction coefficient).

its m. p., and the depression of m. p. observed when it was mixed with punicic or α-elæostearic acid. Recently, Ahlers and Dennison,[13] who examined the infrared spectra of Japanese and Indian snake-gourd oils, suggested that it might be identical with punicic

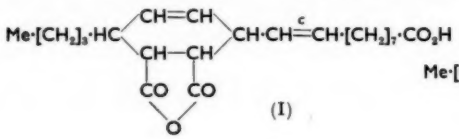
[10] Toyama and Tsuchiya, *ibid.*, 1935, **38**, 185B; contrast Toyama and Uozaki, *ibid.*, 1937, **40**, 249.
[11] Soni and Aggarwal, *J. Sci. Ind. Res., India*, 1949, **8**, *B*, 150.
[12] Farmer and van den Heuvel, *J.*, 1936, 1809.
[13] Ahlers and Dennison, *Chem. and Ind.*, 1954, 603.

acid, or else be a stereoisomer with the orientation of the triene unit reversed relatively to punicic acid.

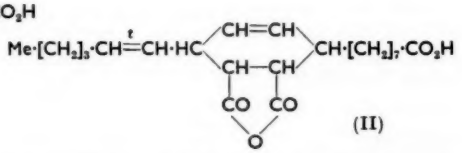
In our hands, Japanese snake-gourd oil yielded an acid, m. p. 43—43·5°, which absorbed three mols. of hydrogen to give stearic acid, and was readily stereomutated to β-elæostearic acid. It depressed the m. p. of α-elæostearic but not punicic acid. Spectroscopic comparison (ultraviolet and infrared solid film) left no doubt that it was identical with the latter. Indian snake-gourd oil, when worked up by a procedure omitting purification by magnesium acetate, also gave an acid of m. p. 43° which showed similar mixed m. p. behaviour. The infrared and ultraviolet data (Table 1) supported the identity with punicic acid but it was observed that ultraviolet intensities were lower than expected, and so were intensities of characteristic infrared bands at 986 and 936 cm.$^{-1}$ (Table 2). These results suggested that there might be a saturated acid as impurity in this sample of trichosanic acid, and this view was strengthened by the low hydrogen uptake and poor analyses. Reversed-phase chromatography [14] then revealed 4% of palmitic and 16% of stearic acid. This Japanese trichosanic acid is thus pure, and Indian trichosanic acid impure, punicic acid. Earlier specimens must have been very impure.

Trichosanic acid being eliminated, we need to know the stereochemistry of α-and β-elæostearic acid and punicic acid before opening synthetic work. Unfortunately, methods for the diagnosis of configuration in trienes are not well established, largely because negligible synthetic work has been carried out and model substances of known configuration are not available. Despite this handicap considerable progress has been made on the octadeca-9 : 11 : 13-trienoic acid system, and this has enabled us to concentrate our synthetic efforts on the correct stereoisomers.

Morrell and Samuels [15] demonstrated that α- and β-elæostearic acid gave different maleic adducts, and showed, by oxidative degradation, that these were (I) and (II) respectively. Morrell and Davis [16] proposed a *cis*-9 : *trans*-11 : *trans*-13-structure for the α-acid and a *trans*-9 : *cis*-11 : *cis*-13-structure for the β-acid, but the reasoning is not fully



(I)



(II)

acceptable as it assumes that *cis*-containing dienes add maleic anhydride with ease.[17] More convincing is the work of Paschke *et al.*[18] which extends that of Chin [19] who used the maleic adducts to support his view that the α-acid is the *cis*-9 : *trans*-11 : *trans*-13- and the β-acid the *trans*-9 : *trans*-11 : *cis*-13-form. They find, by infrared analysis, that the adduct (I) contains an extracyclic *cis*-linkage whilst the isomer (II) has a *trans*-linkage. Since only *trans* : *trans*-dienes add maleic anhydride with ease, α-elæostearic acid is the *cis*-9 : *trans*-11 : *trans*-13- and the β-acid is the *trans*-9 : *trans*-11 : *trans*-13-form. Bickford *et al.*[20] reach similar conclusions and, from a study of the epoxides of the maleic adducts, have found that maleic anhydride adds to β-elæostearic acid at the 11 : 14- as well as the 9 : 12-positions. This, too, supports the all-*trans*-assignment.

[14] Howard and Martin, *Biochem. J.*, 1950, **46**, 532; Crombie, Comber, and Boatman, *ibid.*, 1955, **59**, 309.

[15] Morrell and Samuels, *J.*, 1932, 2251; Rinkes, *Rec. Trav. chim.*, 1943, **62**, 557.

[16] Morrell and Davis, *Trans. Faraday Soc.*, 1936, **32**, 209; *J.*, 1936, 1481.

[17] Contrast, *inter al.*, Robey, Morrell, and Wiese, *J. Amer. Chem. Soc.*, 1941, **63**, 627; Robey, *Science*, 1942, **96**, 47; Craig, *J. Amer. Chem. Soc.*, 1943, **65**, 1006; Snyder, Stewart, and Meyers, *ibid.*, 1949, **71**, 1055; Snyder and Poos, *ibid.*, 1950, **72**, 4104; von Mikusch, *Angew. Chem.*, 1950, **62**, 475; Alder and Vogt, *Annalen*, 1951, **571**, 137; and ref. 22*c*.

[18] Paschke, Tolberg, and Wheeler, *J. Amer. Oil Chemists' Soc.*, 1953, **30**, 97.

[19] Chin, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1950, **53**, 333; *Chem. Abs.*, 1953, **47**, 7435.

[20] Bickford, Du Pré, Mack, and O'Connor, *J. Amer. Oil Chemists' Soc.*, 1953, **30**, 376.

Ahlers *et al.*[21] find that the extinction coefficient of the band at 995 cm.$^{-1}$ in β-elæostearic acid is about three times that of the band at 968 cm.$^{-1}$ in elaidic acid (Table 2), and since the bands are probably similar in origin, commend the all-*trans*-structure. α-Elæostearic acid has two bands in this region (see Table 2). As the band at 992 cm.$^{-1}$ is about twice as strong as that of elaidic acid at 968 cm.$^{-1}$ Ahlers *et al.* suggest that one *cis*-linkage is present and that the configuration is *trans*-9 : *cis*-11 : *trans*-13, *trans*-9 : *trans*-11 : *cis*-13, or *cis*-9 : *trans*-11 : *trans*-13. They discount the first structure on grounds which seem questionable—"... if the two absorption bands noted were presumed to correspond to the two sets of adjacent conjugated pairs of double bonds present, the central *cis*-system might be excluded on symmetry considerations since *cis-trans* and *trans-cis* would not be expected to yield two absorption bands." It is known that a *cis-trans*-diene itself gives two absorption bands in the 1010—930 cm.$^{-1}$ region.[22] Examining pomegranate seed oil,[23] and later punicic acid,[24] Ahlers *et al.* deduced from the ultraviolet data and the extinction coefficient at 988 cm.$^{-1}$ that two *cis*-double bonds were present. This leads to three possible structures—*cis*-9 : *cis*-11 : *trans*-13, *trans*-9 : *cis*-11 : *cis*-13, and *cis*-9-*trans*-11 : *cis*-13. Because the ratio of intensities at 988 cm.$^{-1}$ and 937 cm.$^{-1}$ resembled those of *cis-trans*-conjugated "linoleates," Ahlers *et al.*[23,24] preferred one of the first two structures, but could not distinguish between them.

In the light of this information we felt it reasonable to accept the *cis*-9 : *trans*-11 : *trans*-13-structure for α-elæostearic acid, and the all-*trans*-structure for the β-acid, but rejection by Ahlers and his co-workers of the *cis*-9 : *trans*-11 : *cis*-13-structure for punicic acid seemed unconvincing and we were faced with three possible structures. Our choice for synthesis, *cis*-9 : *trans*-11 : *cis*-13, was based largely on expediency and by good fortune proved to be correct.

The general techniques used for synthesis were developed from Parts II and V and a preliminary note relating to α-elæostearic acid has been published.[25] Hexynylmagnesium bromide with ethyl orthoformate gave 1 : 1-diethoxyhept-2-yne (III),[26] which was semi-hydrogenated and hydrolysed to give hept-*trans*-2-enal (IV) (the *cis*-aldehyde is stereomutated by acid).[27] A Reformatski reaction with propargyl bromide gave dec-1-yn-*trans*-5-en-4-ol (V) containing some allenic material.[28] Unsuccessful attempts to dehydrate an homologous alcohol with toluene-*p*-sulphonic acid or by treating the toluene-*p*-sulphonate with aqueous potassium hydroxide were reported by Hill *et al.*[29] We have found three successful methods for the formal dehydration. Heating the alcohol (V) with phosphorus oxychloride in pyridine gave a 23% yield of deca-3 : 5-dien-1-yne (VI), whilst preparation of the toluene-*p*-sulphonate followed by treatment with sodium *n*-butoxide in butanol gave 30—36% yields. When the alcohol was treated with phosphorus trichloride followed by 15—20% alcoholic potassium hydroxide, the hydrocarbon (VI) was formed in 30% yield. Deca-3 : 5-dien-1-yne was extremely unstable, absorbed 3·85 mols. of hydrogen over a catalyst, and had the expected ultraviolet absorption (Table 3). It is known [30] that treatment of 1-methylbut-3-ynyl toluene-*p*-sulphonate gives a mixture of *cis*- and *trans*-pent-2-en-4-yne when treated with alkali, so comment must be made on the stereochemistry of our material. In the main synthetic work deca-3 : 5-dien-1-yne

[21] Ahlers, Brett, and McTaggart, *J. Appl. Chem.*, 1953, **3**, 433.
[22] (*a*) Jackson, Paschke, Boyd, Tolberg, and Wheeler, *J. Amer. Oil Chemists' Soc.*, 1952, **29**, 229; (*b*) Celmer and Solomons, *J. Amer. Chem. Soc.*, 1953, **75**, 3430; (*c*) Crombie, *J.*, 1955, 1007; (*d*) Allan, Meakins, and Whiting, *J.*, 1955, 1874.
[23] Ahlers and McTaggart, *J. Sci. Food Agric.*, 1954, **2**, 75.
[24] Ahlers, Dennison, and O'Neill, *Nature*, 1954, **173**, 1045.
[25] Crombie and Jacklin, *Chem. and Ind.*, 1955, 1186.
[26] Kranzfelder and Vogt, *J. Amer. Chem. Soc.*, 1938, **60**, 1714; Moureu and Delange, *Bull. Soc. chim. France*, 1904, **31**, 1333.
[27] Raphael and Sondheimer, *J.*, 1951, 2693; Crombie, Harper, and Thompson, *J.*, 1951, 2906.
[28] See Parts II and V for references.
[29] Hill, Lythgoe, Mirvish, and Trippett, *J.*, 1955, 1770.
[30] Bruun, Christensen, Haug, Stene, and Sörensen, *Acta Chem. Scand.*, 1951, **5**, 1244; Allan and Whiting, *J.*, 1953, 3314.

prepared by the phosphorus trichloride route was used and its infrared spectrum was the same as that of the sample from the phosphorus oxychloride procedure. Dehydrochlorinations of this type are known to give *trans*-isomers in other cases [31] and we have no reason to suspect considerable contamination with *cis*-material (cf. dec-3-en-1-yne, Part IV) : nevertheless, this stage is not claimed to be stereospecific. Chain extension of

TABLE 3. *Ultraviolet data for acetylenic intermediates.**†

$Me\cdot[CH_2]_3\cdot CH{=}CH\cdot C{\equiv}CH$	223 (11,000)
$Me\cdot[CH_2]_4\cdot CH{=}CH\cdot C{\equiv}CH$ [a]	222 (10,200)
$Me\cdot[CH_2]_3\cdot CH{=}CH\cdot CH{=}CH\cdot C{\equiv}CH$	260·5 (29,000)
$Me\cdot[CH_2]_4\cdot CH{=}CH\cdot CH{=}CH\cdot C{\equiv}CH$ [b]	260 (30,000)
$Me\cdot[CH_2]_3\cdot C{\equiv}C\cdot CH{=}CH\cdot C{\equiv}CH$	257 (22,500) ; 271 (20,500)
$Me\cdot[CH_2]_3\cdot CH{=}CH\cdot CH{=}CH\cdot C{\equiv}C\cdot[CH_2]_7\cdot Cl$ ...	266·5 (32,000)
$Me\cdot[CH_2]_3\cdot C{\equiv}C\cdot CH{=}CH\cdot C{\equiv}C\cdot[CH_2]_7\cdot Cl$	261 (31,000) ; 276 (30,000)
$Me\cdot[CH_2]_3\cdot CH{=}CH\cdot CH{=}CH\cdot C{\equiv}C\cdot[CH_2]_7\cdot CO_2H$	267 (36,500) [infl. 277 (28,400)]
$Me\cdot[CH_2]_3\cdot C{\equiv}C\cdot CH{=}CH\cdot C{\equiv}C[CH_2]_7\cdot CO_2H$ ...	261 (32,000) ; 276 (30,500)
$Me\cdot[CH_2]_3\cdot CH{=}CH\cdot C{\equiv}C\cdot C{\equiv}C\cdot[CH_2]_7\cdot CO_2Me$	229 (3000) ; 240 (6000) ; 253 (12,500) ; 267 (20,000) ; 283 (15,500)
$Me\cdot CH{=}CH\cdot C{\equiv}C\cdot C{\equiv}CH$ [c]	230 (2250) ; 238 (5000) ; 251 (10,000) ; 264 (14,000) ; 280 (11,000)
$Me\cdot[CH_2]_2\cdot C{\equiv}C\cdot C{\equiv}C\cdot CH{=}CH\cdot CH_2\cdot OH$ [d]	239·5 (7300) ; 252 (14,600) ; 266·5 (21,850) ; 282·5 (19,440)

* Wavelength mμ ; ε in parentheses.
† Infrared data for most of these compounds are given in the Experimental section.
[a] Part V. [b] Bohlmann and Viehe.[28] [c] Armitage *et al.*[25] [d] Bruun *et al.*[26]

sodiodeca-3 : 5-dien-1-yne in liquid ammonia, with 1-chloro-7-iodoheptane,[32] gave 17-chloroheptadeca-5 : 7-dien-9-yne (VII) in 53% yield. The ultraviolet maximum was shifted to 266·5 mμ compared with 260·5 mμ for the monosubstituted dienyne.

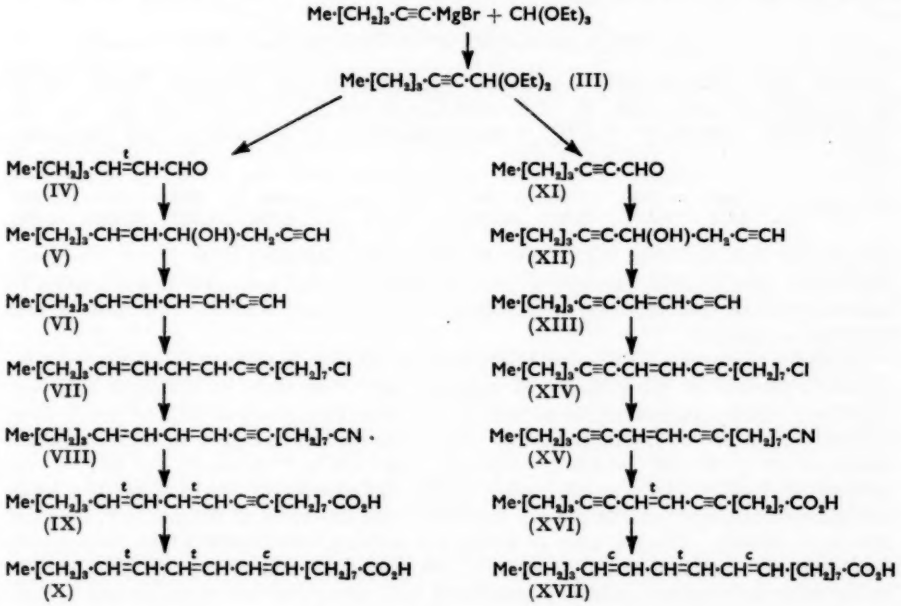
The chloroheptadecadienyne failed to give a Grignard reagent under a variety of conditions, but, by using experience from the ximenynic acid synthesis (Part V), it was possible to convert it into the iodide and then the nitrile (VIII). In subsequent experiments the latter was not isolated but hydrolysed directly to octadeca-11 : 13-dien-9-ynoic acid (IX). The product was a red oil and light-absorption data suggested that it was about 60% pure : it was unchanged by irradiation in light petroleum solution containing iodine. Purification was effected through the urea inclusion compound, and the acid obtained pure and crystalline. On catalytic hydrogenation it absorbed 4 mols. of hydrogen and gave stearic acid. In view of the method of synthesis, its purification by crystallisation and clathrate formation, and its resistance to stereomutation, there is little doubt that octadeca-11 : 13-dien-9-ynoic acid is the *trans-trans*-form. Subsequent synthetic work supports this.

When octadeca-*trans*-11 : *trans*-13-dien-9-ynoic acid was hydrogenated over Lindlar's catalyst [33] in the presence of quinoline until one mol. of hydrogen was absorbed, octadeca-*cis*-9 : *trans*-11 : *trans*-13-trienoic acid (X) was obtained, which, after crystallisation, was identical with α-elæostearic acid (mixed m. p., ultraviolet spectrum, infrared spectrum in CS_2 and as a solid film). When this was treated with iodine, β-elæostearic acid was formed and shown to be identical with a specimen obtained by isomerising the natural acid. We have not carried out a separate synthesis of β-elæostearic acid as the fact that it has a higher m. p. and is a less soluble substance obtained by stereomutating a precursor containing only one *cis*-double bond, adequately confirms its structure and stereochemistry.

For synthesis of punicic acid, hept-2-ynal (XI) was prepared by acid hydrolysis of the acetal (III) and converted by propargylic Reformatski reaction into deca-1 : 5-diyn-4-ol (XII) (containing allene). Treatment with phosphorus tribromide, followed by dehydrohalogenation with 20% alcoholic potassium hydroxide, gave dec-3-ene-1 : 5-diyne (XIII), an extremely unstable substance : after 16 hr. at 0° *in vacuo*, approximately half was lost

[31] *E.g.*, (*a*) Grigor, MacInnes, McLean, and Hogg, *J.*, 1955, 1069; (*b*) ref. 22*c*.
[32] Part V; also Huber, *J. Amer. Chem. Soc.*, 1951, **73**, 2730.
[33] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.

as tar on redistillation. From its method of preparation, we consider that it is largely or entirely in the *trans*-form. The ynenyne system is a new type of chromophore (see Table 3 for data). Chain extension with 1-chloro-7-iodoheptane in liquid ammonia gave 17-chloroheptadec-7-ene-5 : 9-diyne (XIV) (54%). When left in air in the presence of light the substance became dark green, but, when pure, it showed no change *in vacuo* at 0° in subdued light. Conversion of this product (XIV) into the iodide, and then the nitrile, and hydrolysis with 20% aqueous-ethanolic potassium hydroxide, gave a dark

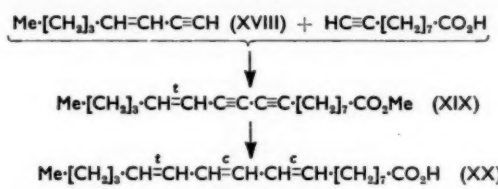


green solid from which octadec-*trans*-11-ene-9 : 13-diynoic acid (XVI) was obtained in colourless plates. It did not form a clathrate compound with urea. The fairly high m. p. (76°) and low solubility in cold light petroleum seem to be consequences of the rigid ynenyne system. The acid was considerably more stable than its relative (IX) and survived exposure to air for 12 hr. at 20° : an explanation may lie in the absence of hydrogen atoms α- to the ethylenic linkage. The structure (XVI) was confirmed by the ultraviolet and infrared data; and on hydrogenation five mols. of hydrogen were absorbed, giving stearic acid. Hydrogenation in ethyl propionate, with Lindlar's catalyst and quinoline, until two mols. of hydrogen had been absorbed, gave octadeca-*cis*-9 : *trans*-11 : *cis*-13-trienoic acid (XVII) which after purification had m. p. 43—43·5° and was identical with punicic (trichosanic) acid (mixed m. p. and infrared criteria). It was stereomutated to β-elæostearic acid.

In view of the opinions of Ahlers *et al.*[23,24] we have made an approach to the synthesis of octadeca-*cis*-9 : *cis*-11 : *trans*-13-trienoic acid (XX). A Reformatski rection between *n*-valeraldehyde and propargyl bromide gave oct-1-yn-4-ol (infrared examination showed allenic impurity). This was converted into the chloride with thionyl chloride and pyridine, but dehydrohalogenation with boiling 15% ethanolic potassium hydroxide was slow. Preparation of the toluene-*p*-sulphonate and treatment with sodamide in liquid ammonia gave oct-3-en-1-yne (XVIII) (55%). Oxidative coupling with dec-9-ynoic acid, followed by distillation, gave only an oil and much tar, in agreement with a report by Black.[34]

[34] Black, Ph.D. Thesis, London, 1955.

The reaction was therefore repeated and the crude acid esterified with diazomethane. Distillation now gave pure methyl octadec-13-ene-9 : 11-diynoate (XIX)



showing the characteristic five-banded spectrum of an enediyne (Table 3).[35,36] In unpublished work with M. Manzoor-i-Khuda we have found that the *cis*- and *trans*-Me·CH=CH·C≡C·C≡C·$[CH_2]_2$·R chromophores have the following light absorptions (mμ) :

cis :	$\lambda_{max.}$ ...	240	253	267	282	*trans* :	$\lambda_{max.}$	239	252	266	282
	ε	4250	8500	12,950	10,700		ε	5500	13,200	19,400	15,000

Comparison indicates that (XIX) must be *trans*-ester containing little, if any, *cis*-isomer. Hydrolysis gave an acid, partially solid at 0°, which was not amenable to purification by low-temperature crystallisation or distillation at 10^{-6} mm. and did not form a urea clathrate compound.

Methyl octadec-*trans*-13-ene-9 : 11-diynoate itself was therefore hydrogenated over Lindlar's catalyst in the presence of quinoline until two mols. of hydrogen had been absorbed. On hydrolysis octadeca-*cis*-9 : *cis*-11 : *trans*-13-trienoic acid (XX) was isolated and further purified by crystallisation at −70°. The acid was a highly unstable crystalline substance, m. p. 35—38°, which decomposed in 14 days at 0° *in vacuo*, and proved very difficult to handle. In the ultraviolet region, octadeca-*cis*-9 : *cis*-11 : *trans*-13-trienoic acid showed only one peak at 271 mμ (ε 32,300) with inflexions at 263 mμ (ε 27,200) and 280 mμ (ε 24,800). When a trace of iodine was added a well-defined triplet immediately developed with maxima at 257 (ε 42,900), 268 (ε 44,400), and 278 mμ (ε 33,000). The latter spectrum is characteristic of β-elæostearic acid, though the intensities are below those for the pure material. This would be explained if the solution contained an equilibrium mixture of stereoisomers, but in view of the m. p. range of 3°, we consider that our specimen was not pure. Nevertheless its infrared spectrum has yielded the data we require, for this stereoisomer could not be confused with punicic acid. α- and β-Elæostearic acid and punicic acid have characteristic bands below 950 $cm.^{-1}$ (compared as solid films or paraffin mulls) which are absent from the spectrum of the *cis*-9 : *cis*-11 : *trans*-13-acid.

In connection with synthetic work on octadeca-9 : 11 : 13-trienoic acids we briefly indicate another type of route which eliminates the chloro-iodide chain extension. Its disadvantage is lack of stereochemical specificity. Ethyl undecenoate was treated with *N*-bromosuccinimide, to give a mixture of two allylic bromides (XXI) and (XXII).[37] Bohlmann and Viehe [38] have demonstrated that mixtures of other allylic bromides can be

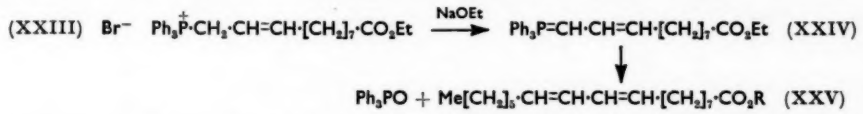
(XXI) CH_2=CH·CHBr·$[CH_2]_7$·CO_2Et Br·CH_2·CH=CH·$[CH_2]_7$·CO_2Et (XXII)

used to give straight-chain isomers in the Wittig reaction,[39] only the primary bromide reacting; so the mixture was treated with triphenylphosphine. The salt was treated with sodium ethoxide in ethanol to form the ester (XXIV), and then with heptaldehyde.

[35] Armitage, Cook, Entwistle, Jones, and Whiting, *J.*, 1952, 1998.
[36] Bruun, Haug, and Sörensen, *Acta Chem. Scand.*, 1950, **4**, 850.
[37] Gensler, Behrmann, and Thomas, *J. Amer. Chem. Soc.*, 1951, **73**, 1071.
[38] Bohlmann and Viehe, *Chem. Ber.*, 1955, **88**, 1245.
[39] Wittig and Schollkopf, *Chem. Ber.*, 1954, **87**, 1318; Wittig and Haag, *ibid.*, 1955, **88**, 1654.

XUM

Distillation of the product gave a diene ester in 23% yield with the expected light absorption max. for the ester (XXV; R = Et). There was no infrared band near 905—915 cm.$^{-1}$, so the product is probably free from vinylic isomer, but bands at 986 and 948 cm.$^{-1}$ show



it to contain *cis-trans*-material. Some of the *cis*-material might originate from the bromo-ester (XXII) as some oleic acid is formed when this reacts with heptylmagnesium bromide.[37] Much probably arises from the Wittig reaction which is known in other cases to give *cis-trans*-mixtures about the newly formed olefinic linkage.[39] Hydrolysis of the mixture of diene esters gave a small yield of octadeca-*trans*-9 : *trans*-11-dienoic acid (XXV; R = H), m. p. 53° (in agreement with recorded data [21, 31a]). Improvements to this preliminary experiment are possible and the use of hept-2-enal or hept-2-ynal could lead to other syntheses of octadeca-9 : 11 : 13-trienoic acids.

Although the syntheses of α- and β-elæostearic and punicic acid may not be fully stereospecific because of the formal dehydration stage, there can now be little doubt about the stereochemistry of these acids. The spectral data given can be safely used for comparison with conjugated trienes of unknown geometrical configuration. It remains to point out a few features of interest. In the ultraviolet spectra, there is a general shift of maximal absorption (~3 mμ) to long wavelengths, accompanied by a decline in extinction coefficient, through the series *trans*-9 : *trans*-11 : *trans*-13, *cis*-9 : *trans*-11 : *trans*-13, to *cis*-9 : *trans*-11 : *cis*-13. (The main maximum for the *cis*-9 : *cis*-11 : *trans*-13- is at the same position as for the *cis*-9 : *trans*-11 : *trans*-13-stereoisomer, but as we have reservations about the purity of the former, it is unprofitable to consider ε.) This general behaviour parallels that of conjugated dienes which show similar variations through the series *trans-trans*, *cis-trans* or *trans-cis*, to *cis-cis*.[40]

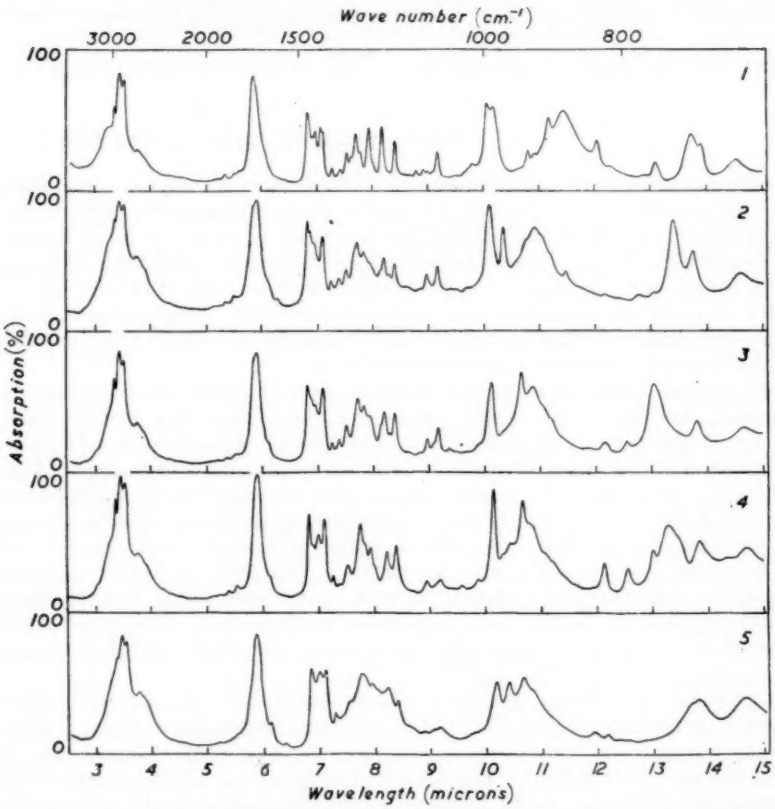
As expected, in solution or a mull, all-*trans*-octadeca-9 : 11 : 13-trienoic acid shows only one strong band in the CH=CH out-of-plane deformation region: *trans-trans*-dienes show similar behaviour, and in both cases the frequency is higher than that of an isolated *trans*-CH=CH bond which absorbs at ~968 cm.$^{-1}$. The band is split in the solid film spectrum (Figure). In the spectra of *cis*-9 : *trans*-11 : *trans*-13- and *cis*-9 : *trans*-11 : *cis*-13-compounds, two bands are present in this out-of-plane deformation region (Table 2, Figure): again *cis-trans*-dienes show a comparable doublet.[22] The *cis*-9 : *cis*-11 : *trans*-13-stereoisomer shows three bands at 987, 965, and 942 cm.$^{-1}$ (solid film; mull spectrum similar).

Our infrared extinction data (except for β-elæostearic acid) agree moderately with those of Ahlers *et al.* only if background absorption is added in. It is clear from the $\varepsilon_2/\varepsilon_1$ columns that there is not an additive contribution to ε for a single isolated *trans*-double bond each time another *trans*-linkage is introduced into a *cis*-triene. The position is worse when correction is made for background absorption (as it should be) than when it is retained. Nevertheless, there is an increasing increment to $\varepsilon_2/\varepsilon_1$ of >1 each time a new *trans*-linkage is introduced, and this fact alone may be of qualitative value.

Crystalline-film spectra for some octadeca-9 : 11 : 13-trienoic acids are shown in the Figure. Specimens were prepared by allowing the compound to melt on warmed rock-salt plates, and then cool to room temperature or 0°. In the case of punicic acid two types of solid-film spectrum (due to differing arrangements of the molecules in the crystal lattice) could be obtained, depending on room temperature. One of the forms (A) could

[40] (*a*) Nichols, Herb, and Riemenschneider, *J. Amer. Chem. Soc.*, 1951, **73**, 247; (*b*) Allan, Jones, and Whiting, *J.*, 1955, 1862; refs. 22*b* and *c*.
[41] Crombie and Tayler, *J.*, 1954, 2816.

Crystalline-film spectra of some octadeca-9 : 11 : 13-trienoic acids.



(1) *trans*-9 : *trans*-11 : *trans*-13 (β-Elæostearic acid). (Peaks at 3095, 2985, 2905, 2835, 2665, 1864, 1806, 1784, 1704, 1464, 1446, 1435, 1414, 1406, 1375, 1346, 1327, 1312, 1299, 1284, 1261, 1225, 1192, 1139, 1123, 1113, 1103, 1092, 1056, 1025, 998, 986, 928, 918, 897, 876, 832, 816, 777, 765, 730, 720, 690 cm.$^{-1}$.)

(2) *cis*-9 : *trans*-11 : *trans*-13 (α-Elæostearic acid). (Peaks at 2995, 2920, 2850, 2660, 1866, 1813, 1698, 1686, 1587, 1465, 1456, 1439, 1408, 1377, 1353, 1328, 1297, 1278, 1271, 1261, 1232, 1222, 1208, 1193, 1166, 1134, 1117, 1093, 1066, 1054, 1036, 993, 969, 931, 918, 908, 874, 822, 784, 767, 746, 728, 685 cm.$^{-1}$.)

(3) *cis*-9 : *trans*-11 : *cis*-13 (A) (Punicic acid). (Peaks at 2985, 2905, 2835, 2655, 1850, 1799, 1685, 1630, 1462, 1455, 1448, 1435, 1406, 1376, 1352, 1329, 1293, 1276, 1258, 1229, 1220, 1204, 1192, 1114, 1101, 1092, 1070, 1009, 989, 938, 920, 894, 823, 797, 768, 725, 683 cm.$^{-1}$.)

(4) *cis*-9 : *trans*-11 : *cis*-13 (B) (Punicic acid). (Peaks at 2990, 2900, 2835, 2655, 1848, 1799, 1692, 1629, 1463, 1446, 1426, 1404, 1376, 1351, 1327, 1291, 1279, 1261, 1250, 1215, 1192, 1120, 1088, 1046, 1014, 987, 971, 958, 938, 925, 904, 891, 825, 797, 769, 754, 723, 696, 678 cm.$^{-1}$.)

(5) *cis*-9 : *cis*-11 : *trans*-13. (Peaks at 2995, 2905, 2835, 2655, 1921, 1704, 1634, 1565, 1462, 1427, 1406, 1376, 1329, 1291, 1261, 1219, 1192, 1128, 1104, 1093, 1026, 987, 965, 942, 839, 822, 733, 726, 684 cm.$^{-1}$.)

be reproduced if cooling was allowed to take place at 0°. Comparison of such spectra is a much more stringent test of identity than solution spectra because the bands are sharper and more numerous. Paraffin mulls are generally satisfactory, though they may be unreproducible if the acid is partially soluble in paraffin.

Experimental

Analyses were carried out in the microanalytical laboratory of Imperial College (Miss J. Cuckney). Infrared measurements were made by Mr. R. L. Erskine, B.Sc., A.R.C.S., using a Grubb-Parsons double-beam instrument; extinction data were determined in CS_2 solutions. Ultraviolet measurements (in pure EtOH) were made with a Unicam S.P. 500 instrument. For many physical data see Tables.

α- and β-Elæostearic Acids.[42]—Tung oil (515 g.) was heated in nitrogen, under reflux, with potassium hydroxide (200 g.) in ethanol (2 l.). The solution was acidified with 2N-sulphuric acid (about 5 l.), then the upper brown layer was washed with hot distilled water (2 × 750 ml.). After 1 hr. at 0° the solid was filtered off and recrystallised four times from ethanol (500 ml. portions) (charcoal) and twice from pentane, to give α-elæostearic acid (186 g.), white plates, m. p. 47—48°. Another crystallisation raised the m. p. to 48°.

β-Elæostearic acid was prepared by adding a crystal of iodine to a solution of the α-form in pentane and setting aside for a few hr. After cooling at 0°, the β-acid was filtered off and when crystallised from ethanol had m. p. 72°.

Punicic Acid.—Pomegranate seeds were washed and dried *in vacuo*. Crushed seeds (18·5 g.) were continuously extracted (3 hr.) with light petroleum (b. p. 40—60°) and then reground and extracted for 5 hr. more. Evaporation of the solvent left a viscous yellow oil (1·45 g.) with maxima at 264 (ε 26,000), 274 (ε 33,000), and 285 mμ (ε 26,000), corresponding to a content of 71% punicic acid. The oil (1·45 g.) was hydrolysed by potassium hydroxide (1·7 g.) in boiling 85% ethanol (25 ml.) for 1 hr. Isolation of the acid with ether, and evaporation *in vacuo*, gave yellow crystals: crystallisation from 80% ethanol (15 ml.) at 0° gave punicic acid (0·87 g.), m. p. 40—42°, raised by two more crystallisations from pentane to m. p. 43·5—44° (white plates) (Found: C, 77·6; H, 11·1. Calc. for $C_{18}H_{30}O_2$: C, 77·65; H, 10·85%). Microhydrogenation 2·95H_2. On hydrogenation stearic acid, m. p. 70°, was obtained, which did not depress the m. p. of an authentic specimen of m. p. 69°. When isomerised with iodine in pentane, punicic acid gave β-elæostearic acid, m. p. and mixed m. p. 71·5°.

Trichosanic acid.—(A) *From Japanese snake-gourd seeds.* Kernels (10·7 g.) were extracted from the cracked gourd seeds (25·1 g.), crushed, and extracted under nitrogen with light petroleum (b. p. 40—60°) for 9 hr. Evaporation of the solvent *in vacuo* gave an oil (5·59 g.). Continued extraction gave no further oil. Japanese snake-gourd oil had maxima at 264 (ε 13,700), 274 (ε 18,500), and 285 mμ (ε 14,300), corresponding to about 44% of the triene. There were infrared bands (liquid film) at 1740s, 989m, and 939m cm.$^{-1}$. Saponification of the oil (5·59 g.) with potassium hydroxide (2·0 g.) in water (2 ml.) and ethanol (18 ml.), by refluxing in nitrogen (2 hr.), gave a crude acid (5·10 g.) which melted below 20°. In accordance with published directions,[10, 11] it was dissolved in 90% ethanol (15 ml.), neutralised to phenolphthalein with 5% potassium hydroxide in 90% ethanol, heated to boiling with a solution of magnesium acetate (1·5 g.) in 90% ethanol (15 ml.), and then set aside at 0° (3 hr.). The precipitated magnesium salts (0·35 g.) were filtered off and rejected. The filtrate was acidified and extracted with ether. The extracts were dried and evaporated, to give an oil which crystallised from 80% ethanol at 0°, giving impure trichosanic acid (1·37 g.), m. p. 35—38°. Two crystallisations from pentane (10 ml.) raised the m. p. to 43—43·5° (long narrow plates) (Found: C, 77·4; H, 11·2%). Microhydrogenation 2·8H_2. Hydrogenation gave stearic acid, m. p. 70° (and mixed m. p.). Iodine-catalysed stereomutation gave β-elæostearic acid, m. p. 71·5° (mixed m. p. and infrared mull comparison).

(B) *From Indian snake-gourd oil.* The gourd seeds (29·7 g.) gave kernels (14·5 g.) which were crushed and extracted with light petroleum (b. p. 40—60°) for 8 hr. under nitrogen, to give the oil (8·59 g.). Ultraviolet maxima were at 264 (ε 16,000), 274 (ε 21,500), and 285 mμ (ε 16,500), corresponding to about 48% of the triene. The oil was hydrolysed (1½ hr.) by boiling 80% ethanol (50 ml.) containing potassium hydroxide (5·0 g.). The acids were isolated with ether in the usual way and obtained semi-solid (8·0 g.). Crystallisation from 80% ethanol at 0° gave trichosanic acid, m. p. 36·5—38·5°, raised by another crystallisation from pentane to 39—41° (2·03 g.). Two similar recrystallisations raised the m. p. to 43° (constant) (Found: C, 77·2; H, 11·4%). Microhydrogenation 2·1H_2. The m. p. was undepressed by admixture with Japanese trichosanic acid or punicic acid. Ultraviolet maxima at 264 (ε 26,400), 274

[42] Thomas and Thompson, *J. Amer. Chem. Soc.*, 1934, **56**, 898.

(ε 36,800), and 285 mμ (ε 28,900). These intensities are 80% of those for punicic acid. Infrared max. (in CS_2) : 986 (ε 124) and 936 cm.$^{-1}$ (ε 82). These intensities are 77% of those for punicic acid and were not increased by recrystallising the trichosanic acid.

A specimen of Indian trichosanic acid (5·9 mg.) was chromatographed on a kieselguhr–paraffin column, elution being with aqueous acetone.[14] Elution was begun at 50% acetone and the concentration increased in 5% steps. Trichosanic acid (4·56 mg.) was eluted in 60%, palmitic acid (0·23 mg.) in 65%, and stearic acid (0·93 mg.) in 70% acetone. The recovery was 5·72 mg. (97%). The composition is thus trichosanic acid 79·7%, palmitic acid 4·1%, and stearic acid 16·2%. These figures are in good agreement with the spectroscopic estimation of punicic acid content and with the analytical data.

1 : 1-*Diethoxyhept-2-yne* (III).—Hexyne, prepared [43] in 64% yield, had b. p. 71—73°, n_D^{19} 1·3995. Hexyne (164 g.) was added to a Grignard reagent prepared by passing methyl bromide vapour into stirred ether (1 l.) containing magnesium (54 g.). The mixture was set aside for 16 hr. and heated under reflux for 1 hr. After cooling, the solution was treated with ethyl orthoformate (320 g.) and then stirred and heated under reflux for 24 hr. The ether was poured off and reserved, the white residue dissolved in iced acetic acid, and the solution extracted with ether. All the ethereal solutions were united and washed with sodium hydrogen carbonate solution and then dried (Na_2SO_4), evaporated, and distilled, to give 1 : 1-diethoxyhept-2-yne (318 g., 86%), b. p. 97—98°/12 mm., n_D^{20} 1·4337. Kranzfelder and Vogt [26] give b. p. 97—98°/10 mm., n_D^{27} 1·4320 (69%).

1 : 1-*Diethoxyhept*-cis-2-*ene*.—1 : 1-Diethoxyhept-2-yne (184·3 g.) was hydrogenated over 3% palladium–barium sulphate in ethyl acetate (200 ml.). When 21·66 l. (N.T.P.) had been absorbed (96·5% of calc. volume for semi-hydrogenation), the reaction was interrupted and the catalyst filtered off. Evaporation and distillation through a 10″ Fenske column gave 1 : 1-*diethoxyhept*-cis-2-*ene* (139 g., 75%), b. p. 86°/10 mm., n_D^{19} 1·4261 (Found : C, 71·35; H, 11·95. $C_{11}H_{22}O_2$ requires C, 70·9; H, 11·9%).

Hept-trans-2-*enal* (IV).—1 : 1-Diethoxyhept-*cis*-2-ene (135 g.) was heated under reflux (45 min.) with water (500 ml.) containing concentrated sulphuric acid (12 ml.) and then steam-distilled (3 hr.). The upper layer was separated and the lower layer twice extracted with ether, and the extracts were united with the upper phase. Drying (Na_2SO_4), evaporation, and distillation through a 12″ Dufton column gave hept-*trans*-2-enal (70 g., 86%), b. p. 70—73°/19 mm., $n_D^{20\cdot5}$ 1·4480. Ultraviolet max. : 219 mμ (ε 13,200) in hexane. Lit.,[44] b. p. 165—167°, n_D^{17} 1·4468.

Dec-5-*en*-1-*yn*-4-*ol* (V).—Zinc (43·5 g.) in dry tetrahydrofuran (120 ml.) was treated with part of a mixture of hept-2-enal (66·6 g.) and propargyl bromide (71·4 g.) in tetrahydrofuran (250 ml.). Mercuric chloride (50 mg.) was added to start the reaction, and then the remainder of the reactants added dropwise. Finally, the product was heated under reflux (15 min.), and set aside overnight. Iced dilute acetic acid was added, and the upper layer separated. The aqueous phase was extracted with ether, and the extracts were added to the upper layer. The ethereal solution was washed with saturated sodium hydrogen carbonate solution and dried (Na_2SO_4). Evaporation and distillation gave *dec*-5-*en*-1-*yn*-4-*ol* (38·0 g., 42%), b. p. 72—75°/0·02 mm., n_D^{23} 1·4642—1·4666 (Found : C, 78·65; H, 10·6. $C_{10}H_{16}O$ requires C, 78·9; H, 10·6%). Microhydrogenation 3·0H_2. There were infrared bands at 3248s (OH), 2123m (C≡CH), 1955m (C=C=C), 1668ms (C=C), and 970s cm.$^{-1}$ (*trans*-CH=CH). The *tetrahydropyranyl ether*, prepared in the usual way, had b. p. 92—96°/0·04 mm., n_D^{22} 1·4682 (Found : C, 76·05; H, 10·3. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·25%).

Deca-3 : 5-*dien*-1-*yne* (VI).—(*A*) Toluene-*p*-sulphonyl chloride (10·0 g.) was dissolved in warm pyridine (5 ml.) and ice-cooled whilst dec-5-en-1-yn-4-ol (7·6 g.) was added with stirring. The product was set aside at 20° overnight and then treated with ice-cold 2N-hydrochloric acid and ether. The ether extracts were washed with dilute acid, and then aqueous sodium hydrogen carbonate, and dried ($MgSO_4$). Evaporation gave an oil (8·8 g.). Sodium (1·37 g.) was dissolved in butan-1-ol (100 ml.), heated to 65°, and mixed with the crude toluene-*p*-sulphonate dissolved in a little butanol. Immediate precipitation and warming occurred. The solution was warmed on a steam-bath (15 min.), then cooled, and pentane (250 ml.) was added. After being washed six times with water, the pentane solution was dried ($MgSO_4$), and the solvent distilled off through a column. Distillation of the residue gave *deca*-3 : 5-*dien*-1-*yne* (2·01 g.,

[43] " Organic Reactions," Vol. V, p. 48.
[44] Delaby and Guillot-Allègre, *Bull. Soc. chim. France*, 1933, **53**, 301.

30%), b. p. 72—74°/12 mm., $n_D^{21\cdot5}$ 1·5022 (Found: C, 88·6; H, 10·75. $C_{10}H_{14}$ requires C, 89·5; H, 10·5%). Ultraviolet max.: 260·5 mμ (ε 25,900).

(*B*) Dec-5-en-1-yn-4-ol (15·2 g.), dissolved in dry pyridine (8 ml.), was stirred at 0° whilst phosphorus trichloride (6·2 g.) in ether (10 ml.) was added dropwise. Stirring was continued for 2½ hr. at 20°, water and ether were then added, and the ethereal extracts washed with 2N-hydrochloric acid, followed by sodium hydrogen carbonate solution. The ethereal solution was dried and evaporated, and the crude chloride (12·8 g.) added to a solution of potassium hydroxide (10 g.) in ethanol (60 ml.). Immediate reaction occurred and the mixture was heated in nitrogen under reflux for 35 min. Working up as usual gave deca-3 : 5-dien-1-yne (4·02 g., 31%), b. p. 56—58°/4 mm., n_D^{27} 1·5040—1·5058. Ultraviolet max.: 260 mμ (ε 29,100). Infrared bands at 3257s, 2101mw (C≡CH), 1932vw (C=C=C), 1638ms (C=C), 1595vw, 1575w, 983s (*trans*-CH=CH), and 943m cm.$^{-1}$ (*trans*-CH=CH conjugated with C≡C). The allene band was very weak.

(*C*) Dec-5-en-1-yn-4-ol (5·45 g.) was dissolved in dry pyridine (10 ml.) and cooled in ice. Phosphorus oxychloride (8 ml.) in dry pyridine (20 ml.) was added dropwise with shaking. After 30 min. the mixture was heated in nitrogen at 100° for 30 min. and then cooled and poured into 2N-hydrochloric acid at 0°. Isolation with ether in the usual way gave, after removal of solvent through a Dufton column and then distillation, deca-3 : 5-dien-1-yne (1·09 g., 23%), b. p. 74—79°/10 mm., n_D^{22} 1·4940—1·4967. Microhydrogenation 3·85H_2. Ultraviolet max.: 260—261 mμ (ε 20,800). The ε value is probably low because the spectrum was not determined immediately. Infrared bands were at 3258s, 2122w, 2098mw, 1637s, 1594vw, 1573w, 984s, and 943m cm.$^{-1}$. There was no allenic absorption.

17-*Chloroheptadeca*-5 : 7-*dien*-9-*yne* (VII).—Deca-3 : 5-dien-1-yne (4·02 g.) in ether (10 ml.) was stirred (5 hr.) with sodamide [from sodium (0·75 g.)] in liquid ammonia (150 ml.). 1-Chloro-7-iodoheptane (8·2 g.) was added, and stirring continued overnight. The ammonia was allowed to evaporate, water and ether were added, and the ethereal extracts washed with water, 2N-hydrochloric acid, and sodium hydrogen carbonate solution. Drying, evaporation, and distillation gave the *chloroheptadecadienyne* (4·06 g., 51%), b. p. 132—135°/0·05 mm., n_D^{31} 1·5112 (Found: C, 76·8; H, 10·5; Cl, 13·9. $C_{17}H_{27}Cl$ requires C, 76·5; H, 10·2; Cl, 13·3%).

Magnesium was activated as follows.[45] Magnesium (4 g.) was covered with dry ether, and iodine (1 g.) added. Reaction occurred with disappearance of the iodine colour. The ether was decanted and the residue heated gently with a Bunsen flame. Iodine was evolved, leaving dull, greyish magnesium which was found to be highly active for preparing octadecylmagnesium chloride. 17-Chloroheptadeca-5 : 7-dien-9-yne (1·08 g.) was dissolved in dry ether (10 ml.), and treated with magnesium. Reaction was not induced, on refluxing, by addition of iodine: after 3 hours' refluxing no Grignard reagent had been formed (Michler's ketone test [46]). In an attempt to facilitate reaction a little methyl iodide was added (immediate reaction) and refluxing continued overnight on a steam-bath. After treatment with carbon dioxide gas (2 hr.) and working up there was no long-chain acidic product, and only recovered chloride (0·68 g.) was isolated. Two further runs gave similar results. The chloroheptadecadienyne was then converted into the bromide with sodium bromide in boiling methanol (nitrogen) [47] and the iodide by similar treatment with sodium iodide in acetone. Both failed to react with magnesium even in the presence of mercuric chloride or methyl iodide.

17-*Cyanoheptadeca*-5 : 7-*dien*-9-*yne* (VIII).—17-Chloroheptadeca-5 : 7-dien-9-yne (217 mg.), sodium iodide (135 mg.), and sodium cyanide (95 mg.) in ethanol (3·0 ml.) and water (0·5 ml.) were heated under reflux (nitrogen) for 41 hr. Isolation of the product gave the *nitrile* (107 mg.), b. p. 148—152°/0·02 mm., n_D^{20} 1·5058 (Found: C, 84·55; H, 10·65; N, 5·2. $C_{18}H_{27}N$ requires C, 84·0; H, 10·6; N, 5·45%). Ultraviolet max.: 266 mμ (ε 26,500). Infrared max.: 2260m (C≡N), 2225w (C≡C), 1639m (C=C), 986s (*trans*-CH=CH), and 941 cm.$^{-1}$ (*trans*-CH=CH conjugated with C≡C).

Octadeca-trans-11 : trans-13-*dien*-9-*ynoic Acid* (IX).—17-Chloroheptadeca-5 : 7-dien-9-yne (4·06 g.), sodium iodide (2·0 g.), and sodium cyanide (2·0 g.) in ethanol (20 ml.) and water (5 ml.) were heated under reflux in nitrogen for 48 hr. Potassium hydroxide (10 g.) in water (25 ml.) was added and refluxing continued for a further 48 hr. The yellow solution was extracted with ether and the extract rejected. Acidification of the aqueous phase, extraction

[45] Underwood and Gale, *J. Amer. Chem. Soc.*, 1934, **56**, 2118.
[46] Gilman and Schulze, *ibid.*, 1925, **47**, 2002.
[47] Bailey and Fujiwara, *ibid.*, 1955, **77**, 165.

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with ether, drying, and evaporation gave an oil (3·68 g., 87%), ultraviolet max. 266 mμ (ε 21,000) (Found : equiv., 283·6. $C_{18}H_{28}O_2$ requires equiv., 276·4). It failed to give a crystalline *S*-benzylthiuronium or benzylamine salt or a *p*-bromophenacyl ester : attempts to distil it caused decomposition. The crude acid (3·68 g.) was dissolved in methanol (40 ml.) containing urea (15 g.) and crystallised at 0°. The clathrate compound was filtered off : when the filtrate was treated with more urea, no further solid was obtained. The clathrate compound was added to dilute acid and extracted with ether. When washed with water, dried, and evaporated, the extracts gave a solid which was twice crystallised from pentane, to give *octadeca*-trans-11 : trans-13-*dien*-9-*ynoic acid* (0·73 g., 20%), m. p. 43—44°, raised by further crystallisation to m. p. 45—46° (Found : C, 78·05; H, 10·2. $C_{18}H_{28}O_2$ requires C, 78·2; H, 10·2%). Microhydrogenation 3·95H_2. The hydrogenation product had m. p. 70°, undepressed when admixed with stearic acid. Infrared bands (solid film) at 2222 (C≡C), 1702 (CO_2H), 1639, 1602 (C=C), 984 (*trans*-CH=CH), and 941 cm.$^{-1}$ (weak : *trans*-CH=CH conjugated with C≡C). The p-*bromophenacyl ester* crystallised from ethanol in plates, m. p. 62—63° (Found : C, 65·35; H, 7·1. $C_{26}H_{33}O_3Br$ requires C, 65·95; H, 7·05%). Treating the dienyne acid (67·2 mg.) with maleic anhydride (25 mg.) in benzene under nitrogen for 20 hr. at 20° and for 7 hr. at 100° gave an oil which failed to crystallise. It was not unchanged acid, being insoluble in light petroleum (b. p. 40—60°).

Octadeca-cis-9 : trans-11 : trans-13-*trienoic* (α-*Elæostearic*) *Acid* (X).—Octadeca-*trans*-11 : *trans*-13-dien-9-ynoic acid (106 mg.), Lindlar's catalyst (115 mg.), and quinoline (33·6 mg.) in ethyl propionate (5 ml.) were treated with hydrogen until 9·40 ml. of hydrogen were absorbed at 24°/719 mm. (95% of that required for semihydrogenation of one acetylenic linkage). The catalyst was removed and the filtrate diluted with ether, washed with 2N-hydrochloric acid, and water, dried, and evaporated. The residue was twice crystallised from pentane, to give *octadeca*-cis-9 : trans-11 : trans-13-*trienoic acid* (21 mg.), m. p. 47°, undepressed by admixture with natural α-elæostearic acid, m. p. 48° (Found : C, 77·4; H, 11·0. $C_{18}H_{30}O_2$ requires C, 77·65; H, 10·85%). Infrared spectrum (solid film) : 1686 (CO_2H), 993, and 969 cm.$^{-1}$ (*trans*-CH=CH in *trans-trans-cis*-conjugated system). The spectrum was identical with that of the natural acid. Isomerisation with iodine gave octadeca-*trans*-9 : *trans*-11 : *trans*-13-trienoic acid, m. p. 71°, undepressed by authentic β-elæostearic acid derived from natural α-acid. The infrared spectrum (paraffin mull) showed bands at 1709s (CO_2H) and 986s cm.$^{-1}$ (*trans*-CH=CH in all-*trans*-conjugated triene system) and was indistinguishable from that of β-elæostearic acid.

Hept-2-*ynal* (XI).—1 : 1-Diethoxyhept-2-yne (100 g.) was heated under reflux in nitrogen with water (350 ml.) containing sulphuric acid (14 g.) for 4 hr. Extraction with ether and purification as usual gave hept-2-ynal (42·5 g., 70%), b. p. 64—67°/15 mm., n_D^{19} 1·4560. Lunt and Sondheimer [48] give b. p. 52—54°/13 mm., n_D^{17} 1·4521 (Found : C, 75·85; H, 9·25. Calc. for $C_7H_{10}O$: C, 76·3; H, 9·15%).

Deca-1 : 5-*diyn*-4-*ol* (XII).—Hept-2-ynal (40 g.) and propargyl bromide (44 g.) in tetrahydrofuran (150 ml.) were added dropwise to zinc wool (32 g.; treated with a little mercuric chloride) in tetrahydrofuran (75 ml.). The product was worked up as described above (see dec-5-en-1-yn-4-ol). Distillation gave *deca*-1 : 5-*diyn*-4-*ol* (24·5 g., 45%), b. p. 79—82°/1 mm., n_D^{19} 1·4729—1·4749 (Found : C, 79·75; H, 9·6. $C_{10}H_{14}O$ requires C, 79·95; H, 9·4%). Microhydrogenation 3·9H_2. The *tetrahydropyranyl ether*, prepared in 89% yield by the usual method, had b. p. 90°/0·05 mm., n_D^{21} 1·4756 (Found : C, 76·7; H, 9·55. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·45%).

Dec-3-*ene*-1 : 5-*diyne* (XIII).—Deca-1 : 5-diyn-4-ol (8·06 g.) was dissolved in ether (15 ml.) and pyridine (1 ml.), cooled in ice, and stirred whilst phosphorus tribromide (4·2 ml.) was added dropwise. After 1 hour's stirring at 0° iced 2N-sulphuric acid was added and the bromide isolated as usual but not distilled. Potassium hydroxide (10 g.) in ethanol (50 ml.) was added and the mixture heated under reflux in nitrogen (15 min.). Working up as usual, the solvent being removed through a Dufton column, gave *dec*-3-*ene*-1 : 5-*diyne* (2·5 g., 35%), b. p. 64—65°/5 mm., n_D^{22} 1·5080—1·5097 (Found : C, 90·4; H, 9·5. $C_{10}H_{12}$ requires C, 90·85; H, 9·15%). Microhydrogenation 4·7H_2. Infrared max. (liquid film) : 3247s (C≡CH), 2336w, 2306w, 2217ms (C≡C), 2105mw (C≡CH), 1589m, 1575w (C=C), 939s cm.$^{-1}$ (*trans*-CH=CH conjugated with C≡C). Weak absorption at 1940 cm.$^{-1}$ suggests a little allenic contaminant.

17-*Chloroheptadec*-7-*ene*-5 : 9-*diyne* (XIV).—Sodamide was prepared from sodium (0·82 g.)

[48] Lunt and Sondheimer, *J.*, 1950, 3361.

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in liquid ammonia (200 ml.; dried over sodium and redistilled), and dec-3-ene-1 : 5-diyne (3·83 g., in ether 20 ml.) was added : the mixture was stirred for 3 hr. 1-Chloro-7-iodoheptane (8·4 g.) was added and the mixture stirred overnight. Ammonium chloride (3 g.) was added, the ammonia allowed to evaporate, and the product isolated with ether. Distillation gave *17-chloroheptadec-7-ene-5 : 9-diyne* (4·16 g., 54%), b. p. 134—138°/10^{-4} mm., n_D^{22} 1·5140—1·5159 (Found : Cl, 13·0. $C_{17}H_{25}Cl$ requires Cl, 13·35%). Infrared max. (liquid film) at 2229m (C≡C) and 937s cm.$^{-1}$ (*trans*-CH=CH conjugated with C≡C). The low frequency of the *trans* out-of-plane deformation mode is noteworthy (see other instances in this paper). The shift caused by conjugation with one acetylenic linkage is still further enhanced.

Octadec-trans-11-*ene*-9 : 13-*diynoic Acid* (XVI).—The preceding chloride (4·16 g.), sodium iodide (2·0 g.), and sodium cyanide (2·0 g.) were heated under reflux in ethanol (20 ml.) and water (4 ml.) in nitrogen for 42 hr. Potassium hydroxide (8·0 g.) in water (20 ml.) was added, and heating continued (24 hr.) until evolution of ammonia ceased. Water and ether were added and the ethereal layer rejected. The aqueous phase was acidified and the crude acid isolated as usual : it was dark green. Recrystallisation from light petroleum (b. p. 60—80°) gave an almost colourless acid (1·743 g., 40%), m. p. 75—76° which became green on the surface whilst being filtered. *Octadec*-trans-11-*ene*-9 : 13-*diynoic acid* was again crystallised and formed white plates, m. p. 76° (Found : C, 78·55; H, 9·6. $C_{18}H_{26}O_2$ requires C, 78·8; H, 9·55%). Microhydrogenation 5·0H_2. Infrared max. (paraffin mull) at 2224mw (C≡C), 1688s (CO_2H), 946ms cm.$^{-1}$ (*trans*-CH=CH conjugated with C≡C). Hydrogenation gave stearic acid, m. p. 70° (and mixed m. p.). The enediyne did not form a urea complex.

Octadeca-cis-9 : trans : 11-cis-13-*trienoic Acid* (XVII).—Octadec-*trans*-11-en-9 : 13-diynoic acid (446 mg.) was hydrogenated in ethyl propionate (25 ml.) over Lindlar's catalyst (434 mg.) in the presence of quinoline (145 mg.) until hydrogen (81·5 ml. at 24°/736 mm.) had been absorbed (semihydrogenation of the two acetylenic linkages needs 81·6 ml.). The catalyst was removed and the filtrate diluted with ether, washed with 2N-hydrochloric acid and water, dried ($MgSO_4$), and evaporated. One crystallisation from pentane gave *octadeca*-cis-9 : trans-11 : cis-13-*trienoic acid* (0·313 g., 70%), m. p. 35—38° raised by one recrystallisation to 41° (0·175 g.), and by two further crystallisations to m. p. 43—43·5° (Found : C, 77·4; H, 10·8%). The acid crystallised in needles or plates. Infrared bands (CS_2) at 987 cm.$^{-1}$ (ε 154) and 937 cm.$^{-1}$ (ε 104) (cf. Table 2). The m. p. was undepressed on admixture with natural punicic (m. p. 43·5—44°) or trichosanic (m. p. 43—43·5°) acid. The infrared spectra of all three acids, compared as solid films or in CS_2 solution, were identical. The synthetic acid was isomerised in pentane solution with iodine to β-elæostearic acid, m. p. 71° (from ethanol) undepressed by the naturally derived acid.

Oct-1-yn-4-ol.—A Reformatski reaction between valeraldehyde (32 g.) and propargyl bromide (45 g.) in dry tetrahydrofuran (200 ml.), by use of zinc (29·5 g.) covered with tetrahydrofuran (150 ml.), gave *oct-1-yn-4-ol* (19·8 g., 42%), b. p. 77—85°/10 mm., n_D^{20} 1·4462—1·4485 (Found : C, 75·7; H, 11·35. $C_8H_{14}O$ requires C, 76·15; H, 11·2%). Infrared bands were at 3384s (OH), 3300s, 2128m (C≡CH), and 1963m cm.$^{-1}$ (C=C=C).

Oct-3-en-1-yne (XVIII).—The toluene-*p*-sulphonate was prepared from oct-1-yn-4-ol (19·8 g.), by means of toluene-*p*-sulphonic acid (30·8 g.) and pyridine (12·4 ml.). The crude red oil (39·4 g., 89%) was added in ether (50 ml.) to sodamide [from sodium (7·6 g.)] in liquid ammonia (250 ml.), and the mixture stirred for 5 hr. Ammonium chloride (20 g.) and water (250 ml.) were added and the mixture worked up in the usual way, to give *oct-3-en-1-yne* (8·4 g., 55%), b. p. 126—128°, n_D^{22} 1·4431 (Found : C, 88·5; H, 11·35. C_8H_{12} requires C, 88·8; H, 11·2%). Infrared bands at 3268s, 2112w (C≡CH), 1616w (CH=CH), and 960m cm.$^{-1}$ (*trans*-CH=CH conjugated with C≡CH). There was no allenic absorption. Black [34] gives b. p. 72—73°/110 mm., n_D^{25} 1·4430—1·4440, but prepared the compound by a different procedure.

Oct-1-yn-4-ol (21 g.) and pyridine (13 ml.) were cooled to −10° and thionyl chloride (24·7 g.) added dropwise, with stirring. After 12 hr., the mixture was worked up in the usual way, to give 4-chloro-oct-1-yne (13·7 g., 58%), b. p. 90—105°/40 mm., n_D^{20} 1·4500—1·4510. Attempts to dehydrochlorinate this chloride with 15% ethanolic potassium hydroxide gave only small yields of impure oct-3-en-1-yne.

Methyl Octadec-trans-13-*ene*-9 : 11-*diynoate* (XIX).—Oct-3-en-1-yne (8·4 g.) and dec-9-ynoic acid (13 g.) in methanol (250 ml.) were mixed with a solution of cuprous chloride (33 g.) and ammonium chloride (100 g.) in 0·08N-hydrochloric acid (250 ml.). After 80 minutes' shaking in oxygen, gas absorption ceased (approx. 3 l. used). The solution was acidified and

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extracted with ether. The ether solutions were extracted with alkali, and the acidic product isolated in the usual way and esterified with diazomethane. Distillation gave *methyl octadec*-trans-13-*ene*-9 : 11-*diynoate* (5·47 g., 24%), b. p. 137—141°/0·001 mm., n_D^{19} 1·5129 (Found : C, 78·65; H, 9·85. $C_{19}H_{28}O_2$ requires C, 79·1; H, 9·8%). Infrared bands at 2242mw (C≡C), 2146w, 1737s (CO_2Me), 956m cm.$^{-1}$ (*trans*-CH=CH conjugated with C≡C).

The ester (5·45 g.) was hydrolysed with potassium hydroxide (5·0 g.) in ethanol (45 ml.) and water (5 ml.), but the acid produced was an uncrystallisable yellow oil which failed to form a urea complex. Re-esterification gave methyl octadec-13-ene-9 : 11-diynoate, b. p. 132—134°/0·001 mm., n_D^{22} 1·5112.

Partial Hydrogenation of Methyl Octadec-trans-13-*ene*-9 : 11-*diynoic Acid*.—The enediyne ester (1·145 g.) was hydrogenated in ethyl propionate (50 ml.) over Lindlar's catalyst (1·128 g.) in the presence of quinoline (0·35 ml.) until hydrogen (190 ml. at 25·5°/730 mm.) had been absorbed (202 ml. required for semihydrogenation of the two acetylenic linkages). The catalyst was filtered off, leaving an oil. Ultraviolet max. : 271 mμ (ε 22,500), with inflexions at 264—265 (ε 19,600) and 279—280 mμ (ε 17,400). Saponification of the crude ester, by potassium hydroxide (1·5 g.) in 90% ethanol (15 ml.) under reflux in nitrogen, gave the crude acid which was dissolved in 80% ethanol (10 ml.) and cooled to 0°. A small quantity of solid was removed. The filtrate was evaporated *in vacuo* and the residual oil dissolved in pentane (10 ml.) and crystallised at −70°. A solid (0·32 g.) was obtained which after further low-temperature crystallisation from pentane had m. p. 35—38°. Attempts to form a urea complex from the filtrate from the first pentane crystallisation gave a solid product which on decomposition yielded only an oil (0·26 g.) at 20° (solid at 0°). Repetition of this experiment gave a similar triene acid, m. p. 35—39°, with ultraviolet max. 271 mμ (ε 30,000). The acid was extremely unstable.

Octadeca-9 : 11-*dienoic Acid* (XXV; R = H).—A mixture of ethyl 11-bromoundec-9-enoate (XXII) and ethyl 9-bromoundec-10-enoate (XXI) was prepared according to directions in the literature.[37] The mixed bromo-esters (4·2 g.) and triphenylphosphine (4·2 g.) were dissolved in benzene (20 ml.) and set aside for 48 hr. On dilution with ether (50 ml.) a colourless oil was precipitated which solidified at 0°. It was dissolved in benzene, then reprecipitated with ether, and the solvent was decanted. The residual oil (6·4 g.) was dissolved in dry ethanol (30 ml.) and treated with sodium ethoxide [from sodium (0·27 g.)] in ethanol (15 ml.). After 16 hr. *n*-heptaldehyde (1·6 ml.) was added and the mixture again set aside (16 hr.). Most of the solvent was removed *in vacuo*, 2N-hydrochloric acid added, and the solution extracted with ether. After evaporation of the ether extract, pentane was added and triphenylphosphine oxide filtered off. Evaporation and distillation gave a fraction, b. p. 80—83°/5 × 10^{-3} mm., n_D^{21} 1·4528 (0·8 g.), and ethyl octadeca-9 : 11-dienoate (0·846 g., 19%), b. p. 118—120°/5 × 10^{-4} mm., n_D^{21} 1·4772. A little triphenylphosphine oxide was slowly deposited from the latter fraction and the ester was decanted. Ultraviolet max. 230—232 mμ (ε 24,500). It had infrared bands at 1733s (CO_2Et), 985m, and 948mw cm.$^{-1}$ (*trans-cis*-diene). There was no vinyl absorption at 905—915 cm.$^{-1}$. On hydrolysis in 90% ethanol (5 ml.) containing potassium hydroxide (0·59 g.), under reflux (1 hr.), the ester (0·54 g.) gave an oily acid. Crystallisation from light petroleum (b. p. 40—60°) (charcoal) gave octadeca-*trans*-9 : *trans*-11-dienoic acid, m. p. 53·5° (Found : C, 76·9; H, 11·8. Calc. for $C_{18}H_{32}O_2$: C, 77·1; H, 11·5%). Ultraviolet max. 231 mμ (ε 36,000). Infrared bands (mull) : 1709s (CO_2H), 982s cm.$^{-1}$ (*trans-trans*-diene). Lit.,[21,31a] m. p. 53—54°, ultraviolet max. 232 mμ (ε 32,000). The filtrate from the crystallisation contained a mixture of acids (presumably stereoisomers) which was solid at 0°; they were not further investigated.

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Department of Chemistry,
Imperial College of Science and Technology,
South Kensington, London, S.W.7.

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312. *Further Investigations in the Butenyl–Boron Trichloride System.*

By W. Gerrard, M. F. Lappert, and H. B. Silver.

The present together with earlier work [1,2] constitutes a systematic investigation of the reactions of boron trichloride with allylic alcohols, ethers, and borates, and of the properties of allylic borates, chloroboronates, and dichloroboronites. The systems now reported are the 1- and the 3-methylallyl. For comparison with a non-allylic system, certain analogous reactions involving but-3-enyl compounds were also carried out. The results are discussed and it is concluded that the 1- and the 3-methylallyl group have electron-releasing power (3- > 1-) intermediate between those of typical *sec.*- and *tert.*-alkyl groups; by contrast the but-3-enyl is scarcely more electron-releasing than the *n*-butyl group. Allylic rearrangements producing methylallyl chlorides were observed and are considered to be of S_Ni' type; an alcoholysis with tri-3-methylallyl borate indicated C–O fission.

The present paper supplements our earlier studies [1,2] of the interaction of boron trichloride and allylic alcohols, ethers, and borates and of the properties of allylic borates $B(OR)_3$, chloroboronates $BCl(OR)_2$, and dichloroboronites $BCl_2{\cdot}OR$. Previously, the allyl, 2-methylallyl, and prop-2-ynyl systems were reported: [1,2] the present investigation is concerned with the 1- and 3-methylallyl and the but-3-enyl system. These reactions are now available for comparison with corresponding ones involving saturated compounds.[3–8] Our purpose has been to demonstrate the influence of the allylic double bond on the reactivity of the 1-carbon atom, to show how this is modified when a methyl group is present in the 1-, 2-, or 3-position, to indicate how this effect is further modified when the double bond is in a more remote position (but-3-enyl system), and to obtain information regarding the mechanisms of those reactions wherein C–O fission was possible, by noting any anionotropic changes in the 1- and 3-methylallyl systems.

Tri-1- and -3-methylallyl borate were prepared from boric acid, benzene, and the appropriate alcohol [for a discussion of this method see ref. (9)]. Attempted preparation of the same borates from boron trichloride [see (1)] using the conventional technique [see ref. (9)] was unsuccessful, reaction (2) being observed instead.* Tri-1-methylallyl borate was however obtained in 58% yield, when the formed hydrogen chloride was removed instantly at low temperature and no solvent was present. The conventional method provided a nearly quantitative yield of tribut-3-en-1-yl borate.

$$(1) \qquad BCl_3 + 3ROH \longrightarrow B(OR)_3 + 3HCl$$

$$(2) \qquad BCl_3 + 3ROH \longrightarrow 3RCl + B(OH)_3$$

Tri-1- and -3-methylallyl borates were readily hydrolysed [see (3)], and reacted with octan-1-ol [see (4)], whereas with hydrogen chloride there was no reaction at room temperature; at 110°, however, tri-3-methylallyl borate was dealkenylated [see (5)].

* The composition (*i.e.*, relative percentages of 1- and 3-methylallyl compounds) of the product is shown in Table 2 and similarly for subsequent reactions involving 1- and 3-methylallyl derivatives.

[1] Gerrard, Lappert, and Silver, *J.*, 1956, 3285.
[2] *Idem*, *J.*, 1956, 4987.
[3] Gerrard and Lappert, *J.*, 1951, 1020.
[4] *Idem*, *ibid.*, p. 2545.
[5] Lappert, *J.*, 1956, 1768.
[6] Gerrard and Lappert, *J.*, 1955, 3084.
[7] Lappert, *J.*, 1953, 667.
[8] Gerrard and Lappert, *J.*, 1952, 1486; Edwards, Gerrard, and Lappert, *J.*, 1955, 1470; 1957, 377; Abel, Edwards, Gerrard, and Lappert, *J.*, 1957, 501.

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Interaction between boron trichloride and the borates in the proportions indicated by schemes (6) and (7) afforded alkenyloxyboron chlorides only in the but-3-enyl system; these were reasonably stable at room temperature. With the methylallyl borates the

$$B(OR)_3 + 3H_2O \longrightarrow 3ROH + B(OH)_3 \quad (3)$$

$$B(OR)_3 + 3C_8H_{17}\cdot OH \longrightarrow B(O\cdot C_8H_{17})_3 + 3ROH \quad (4)$$

$$B(OR)_3 + 3HCl \longrightarrow 3RCl + B(OH)_3 \quad (5)$$

isolated products indicated instant decomposition according to schemes (8) and (9). Attempts to show that alkenyloxyboron chlorides had been formed, by preparing (stable) pyridine complexes at −80°, was successful only for di-1-methylallyl chloroboronate.

$$2B(OR)_3 + BCl_3 \longrightarrow 3BCl(OR)_2 \quad (6)$$

$$B(OR)_3 + 2BCl_3 \longrightarrow 3BCl_2\cdot OR \quad (7)$$

$$3BCl(OR)_2 \longrightarrow 3RCl + B_2O_3 + B(OR)_3 \quad (8)$$

$$3BCl_2\cdot OR \longrightarrow 3RCl + B_2O_3 + BCl_3 \quad (9)$$

Di-3-methylallyl ether was cleaved at low temperature by boron trichloride [see (10)].

$$3R_2O + 2BCl_3 \longrightarrow 6RCl + B_2O_3 \quad (10)$$

3-Methylallyl chloride was not affected by a trace of boron trichloride in one hour at room temperature, but a larger quantity catalytically effected addition-polymerisation. Double-bond estimation of this material, if considered as a means of end-group analysis, indicates a molecular weight of about 1450 for the product.

Discussion.—By experiments with boron compounds and allyl derivatives, we had shown [2] qualitatively that the electron-releasing power of the allyl group is intermediate between that of a primary and a secondary alkyl group. The present experiments with methylallyl compounds show that methyl substitution in the 1- or 3-position markedly increases electron-release (in contrast to substitution in the 2-position [1]), and that generally the relative electron-release of the 1- and the 3-methylallyl group is intermediate between those of a typical *sec.*-alkyl (*e.g.*, *sec.*-butyl) and a typical *tert.*-alkyl (*e.g.*, *tert.*-butyl) group. Moreover, the 3-methylallyl group (a primary one) appears to be more powerfully electron-releasing than its 1-isomer (a secondary one). Our conclusions may be compared with those, based on kinetic data obtained by studying certain reactions of allylic chlorides, of Oae and Werf,[10] Andrews and Young,[11] and Vernon.[12] Our conclusion with respect to the 1- and the 3-methylallyl group supports the earlier work,[10, 11] and not the later.[12] The results in the but-3-enyl system indicate that an olefinic double bond in the 3-position has little effect on the reactivity of the 1-carbon atom, although it appears that the but-3-enyl group is more powerfully electron-releasing than *n*-butyl. Our interpretation of reactivites is based on comparison of the reactions here described with analogous ones in saturated systems; the relevant data are summarised in Table 1. Further evidence in the methylallyl systems is based on our conclusion that in most of the reactions (see Table 2) where C–O fission was possible a carbonium cation was in fact an intermediate (S_N1' reaction), whereas most of the corresponding reactions with typical *sec.*-alkyl compounds involved S_N2 replacement on the 1-carbon atom, as demonstrated mainly by studies of Walden inversion.[3]

From Table 2 it is evident that the relative composition of the methylallyl chlorides, obtained from the reactions described, is constant (R^3Cl, 66·5 ± 2·5%; R^1Cl, 33·5 ± 2·5%; R^3 and R^1 = 3- and 1-methylallyl respectively) irrespective of the nature (*i.e.*, 1- or 3-methylallyl) of the starting compounds. This can only reasonably be accounted for by

[9] Lappert, *Chem. Rev.*, 1956, **56**, 959.
[10] Oae and VanderWerf, *J. Amer. Chem. Soc.*, 1953, **75**, 2724.
[11] Andrews and Young, *ibid.*, 1944, **66**, 421.
[12] Vernon, *J.*, 1954, 423.

TABLE 1.

Reaction	Results		Ref.
	Typical primary or *sec.*-alkyl	Typical *tert.*-alkyl	
$BCl_3 + 3ROH$ ...	Scheme (1)	Scheme (2)	3, 4
Schemes (3) & (4)	Reaction involves B–O fission	Reaction mechanism may involve C–O fission (not yet demonstrated)	3, 13
Scheme (5)	No reaction	Rapid reaction at 20°	3, 4
Scheme (8)	Chloroboronates are stable at 20° (primary more stable than secondary at high temperature)	No evidence for existence of chloroboronate	5
Scheme (9)	Primary dichloroboronites stable at 20°, unlike secondary which, however, at −80° form stable complexes with pyridine	No evidence for existence of dichloroboronite	6, 7

TABLE 2.*

Allylic rearrangements were observed in the 1- and 3-methylallyl systems in the reactions listed.

Reaction no.	3	5	5	6	9	9	11
R in reactant	R^3	R^3	R^1	R^3	R^1	R^3	R^3
Composition of product (%)	R^3Cl 68 R^1Cl 32	R^3OH 91·3 ± 0·5 R^1OH 8·7 ± 0·5	R^1OH 100	R^3Cl 69 R^1Cl 31	R^3Cl 69 R^1Cl 31	R^3Cl 66 R^1Cl 34	R^3Cl 64 R^1Cl 36

* R^1 and R^3 = 1- and 3-methylallyl.

assuming that each reaction involves an intermediate carbonium cation (11), which being mesomeric, is identical irrespective of the nature of the source, that is to say each reaction is of S_Ni' type.[14] These conclusions support our earlier views that the analogous reactions

(11) $CH_3{-}CH{=}CH{-}CH_3^+ \longleftrightarrow \overset{+}{C}H_2{-}CH{-}CH{=}CH_2$

in saturated systems, when involving strongly electron-releasing alkyl groups, proceeded by S_Ni mechanisms. The formation of the carbonium cation in the decomposition of the alkenyloxyboron chlorides, and in the dealkenylation of tri-3-methylallyl borate substantiate the mechanisms previously suggested.[3-6] The present results are similar to those of Catchpole and Hughes;[15] by ethanolysis of 1- and 3-methylallyl chlorides, under conditions favouring pre-ionisation, identical mixtures of ethers were obtained. The isolation of a mixture of methylallyl chlorides, having the above composition, in a future investigation may be used as evidence of an S_Ni' reaction.

Experiments on esterification, hydrolysis, and alcoholysis, with one exception (see Table 2), did not lead to rearranged products. This suggests that these reactions involved B–O and not C–O fission. The exception was alcoholysis (octan-1-ol) of tri-3-methylallyl borate; the result suggests that some C–O fission was involved. This is the first example of such a reaction in the boron system.

The effect of boron trichloride on 3-methylallyl chloride is probably understandable in terms of a standard cationic polymerisation mechanism. Thus the 3-methylallyl chloride may, in the first instance, be functioning as co-catalyst, producing with boron trichloride a carbonium cation, which is then available for initiation of polymerisation [cf. ref. (16)].

EXPERIMENTAL

Preparations and Techniques.—3-Methylallyl alcohol was prepared by Nystrom and Brown's procedure[17] (reduction of crotonaldehyde with lithium aluminium hydride); a by-product,

[13] Scattergood, Miller, and Gammon, *J. Amer. Chem. Soc.*, 1945, **67**, 2150.
[14] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953, p. 586.
[15] Catchpole and Hughes, *Trans. Faraday Soc.*, 1941, **37**, 629.
[16] Pepper, *Quart. Rev.*, 1954, **8**, 88.
[17] Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 1197.

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not previously reported, was di-3-methylallyl ether, the identity of which was established analytically and by infrared spectroscopy. But-3-en-1-ol was obtained in low yield by passing formaldehyde vapour into allylmagnesium bromide and conventional working-up. Procedures for purification of starting materials and analytical methods have been described previously.[1,2,3] Mixtures of 1- and 3-methylallyl chloride were analysed by the refractive-index method,[18] and of 1- and 3-methylallyl alcohols by infrared spectroscopy. As the composition of mixtures has been given in Table 2, such mixtures will be referred to non-committally in the experimental part as butenyl chlorides or alcohols.

Preparation of Borates.—A mixture of the alcohol (3 moles), boric acid (1 mole), and benzene (30 c.c.) was carefully fractionated, a modified Dean and Stark head being used for removal of the first fraction, comprising the benzene–water azeotrope, and subsequently a total-reflux partial take-off head for separation of the succeeding fractions (benzene and *borate*). The results are shown in Table 3.

TABLE 3.

R in $B(OR)_3$	Yield (pure) (%)	B. p./mm.	$n_D^{t°}$	$d_D^{t°}$	Found (%) C	H	B	Required (%) C	H	B
1-Methylallyl ...	73	78°/10	(20)1·4177	(18)0·8717	64·7	9·2	4·8	64·4	9·4	4·8
3-Methylallyl ...	81	112°/9	(25)1·4428	(15·5)0·9160	64·5	9·2	4·8	64·4	9·4	4·8

Interaction of Alcohols and Boron Trichloride [*Reactions* (1) *and* (2)].—(a) *But-3-en-1-ol.* The trichloride (4·30 g., 1 mol.) in *n*-pentane (10 c.c.) at −35° was added during 10 min. to the alcohol (8·11 g., 3 mols.) in *n*-pentane (25 c.c.) at −80°. Volatile matter was removed at 20°/15 mm. and subsequent distillation afforded *tribut-3-en-1-yl borate* (7·89 g., 94%), b. p. 112°/15 mm., n_D^{20} 1·4332, d_4^{22} 0·8925 (Found: C, 64·4; H, 9·4; B, 4·8%).

(b) *1-Methylallyl alcohol.* The trichloride (3·09 g., 1 mol.) in *n*-pentane (10 c.c.) at −35° was added during 15 min. to 1-methylallyl alcohol (5·70 g., 3 mols.) in *n*-pentane (20 c.c.) at −80°. The resulting mixture, a white solid and a colourless liquid, was warmed to 20° and kept at this temperature for 15 hr. Volatile matter was removed at 20°/15 mm. and subsequent distillation of the remainder (3·40 g.) afforded impure tri-1-methylallyl borate (0·32 g., 4·6%), b. p. 40—43°/14 mm. (Found: B, 3·01%), and a residue of boric acid (1·53 g., 94%).

The experiment was repeated with identical procedure, except that volatile matter wa s removed directly after completion of addition; this gave 15·1% of borate. When no solvent was used, however, and again volatile matter was rapidly removed, the borate was obtained in 58% yield.

(c) *3-Methylallyl alcohol.* The alcohol (8·76 g., 3 mols.) was added during 40 min. to the trichloride (4·75 g., 1 mol.) at −80°; the reaction was violent and boron trichloride (0·68 g.) which escaped was collected. Butenyl chloride (6·70 g., 70%), n_D^{25} 1·4263 (Found: Cl, 39·3. Calc. for C_4H_7Cl: Cl, 39·3%), was collected as a condensate at −80° and a residue of boric acid (2·11 g., 98%) was obtained after the mixture had been at 18°/5 mm.

Chemical Properties [*Reactions* (3)—(5)] *of Borates.*—(a) *Hydrolysis.* When water (0·54 g., 1 mol.) was added to tri-1- and tri-3-methylallyl borate (2·24 g., 3 mols.) severally and the mixture evacuated at 20°/0·01 mm., the corresponding alcohol (96·3% and 99%, respectively) was obtained as a condensate at −80°, leaving boric acid (100%) as a residue.

(b) *Alcoholysis.* Octan-1-ol (7·80 g., 3 mols.) was added to each borate (4·48 g.) severally. Tri-1-methylallyl borate afforded 1-methylallyl alcohol (4·19 g., 97%) as a condensate, tri-*n*-octyl borate (5·75 g., 72·3%), b. p. 222°/28 mm., and a residue (1·01 g.), whereas tri-3-methylallyl borate, after similar working-up, gave butenyl alcohol (3·74 g., 87%), n_D^{20} 1·4250, and tri-*n*-octyl borate (7·33 g., 92%), b. p. 178°/0·25 mm. (Found: B, 2·71. Calc. for $C_{24}H_{51}O_3B$: B, 2·72%).

(c) *Dealkenylation.* Tri-1-methylallyl borate was recovered quantitatively, after hydrogen chloride had been passed into it continuously at 18° (1 hr.) and subsequently at 120° (4 hr.).

Tri-3-methylallyl borate did not react with hydrogen chloride at 15° during 10 hr. When the gas was passed through this borate (7·21 g.) at 110° (4 hr.), boric acid (1·97 g., 99%) remained in the reaction vessel and butenyl chloride (6·10 g., 70%), n_D^{20} 1·4290 (Found: Cl, 39·2%), was collected in a trap at −80°.

Interaction between Trialkenyl Borates and Boron Trichloride [*Reactions* (6) *and* (7)].—(a) *But-3-en-1-yl.* The trichloride (0·90 g., 1 mol.) was added to the borate (3·44 g., 2 mols.)

[18] Eisner and Young, *ibid.*, 1941, **63**, 2113.

at −80°, whereupon *dibut-3-en-1-yl chloroboronate* was formed in quantitative yield; it had b. p. 47°/0·2 mm., n_D^{20} 1·4338, d_4^{23} 0·9745 (Found: Cl, 18·4; B, 5·78. $C_8H_{14}O_2ClB$ requires Cl, 18·8; B, 5·74%).

By similar procedure, *but-3-enyl dichloroboronite* was obtained quantitatively from boron trichloride (2·70 g., 2 mols.) and the borate (2·58 g., 1 mol.); it had b. p. 36°/15 mm., n_D^{20} 1·4261 (Found: Cl, 44·5; B, 7·01. $C_4H_7OCl_2B$ requires Cl, 46·4; B, 7·08%).

(b) *1- and 3-Methylallyl.* Attempted preparation of the chloroboronates and dichloroboronites by means of reactions (6) and (7) was unsuccessful owing to the low stability [see reactions (8) and (9)] of these compounds. Thus when each borate (2 mols.) was mixed at −80° with boron trichloride (1 mol.), a sample withdrawn from each mixture revealed that 94—95% decomposition according to scheme (8) had taken place within 1 min. at 20°; this was determined by analysis.

When tri-1-methylallyl borate (2·43 g., 1 mol.) was added to boron trichloride (2·55 g., 2 mols.) at −80° a vigorous reaction occurred. The mixtures was warmed to 20°. After 8 hr. at 20°/20 mm., boron trichloride (0·96 g.) was collected in a potassium hydroxide absorption tube, and a solid brown residue (3·75 g.) (Found: Cl, 6·57; B, 2·48%) remained; this was insoluble in water. We interpret this result as decomposition of 1-methylallyl dichloroboronite first formed, according to (9), followed by polymerisation of 1-methylallyl chloride by boron trichloride, a reaction independently demonstrated for the 3-isomer (see below).

Pyridine Complexes of Methylallyloxyboron Chlorides.—Pyridine (3·44 g., 3 mols.) in *n*-pentane (5 c.c.) was added to a mixture of tri-1-methylallyl borate (6·49 g., 2 mols.) and boron trichloride (1·70 g., 1 mol.) in *n*-pentane (5 c.c.) at −80°. The mixture was warmed to 20° and volatile material was removed at 20°/15 mm. The residue was washed with more *n*-pentane. Removal of solvent afforded the impure solid 1 : 1-*complex* between pyridine and di-1-methylallyl chloroboronate (8·95 g., 77%) (Found: Cl, 9·7; C_5H_5N, 29·6. $C_{13}H_{19}O_2NClB$ requires Cl, 13·2; C_5H_5N, 29·7%).

Attempted preparation, by a similar technique, of pyridine complexes of 1-methylallyl dichloroboronite and of the 3-methylallyloxyboron chlorides proved unsuccessful.

Decomposition (8) of Bismethylallyl Chloroboronates.—(a) *The 1-isomer.* Boron trichloride (3·10 g., 1 mol.) at −80° was added to tri-1-methylallyl borate (11·85 g., 2 mols.) at −80°. The mixture was warmed to 20° and, whilst in series with a cold-trap at −80°, was heated for 1 hr. at 135°, then cooled to 20° and evacuated at 20°/20 mm. Butenyl chloride (4·42 g., 62%), $n_D^{22\cdot5}$ 1·4276 (Found: Cl, 39·0%), was collected in the trap. The remainder afforded on distillation tri-1-methylallyl borate (5·00 g., 85%), b. p. 74°/10 mm. (Found: B, 4·86%), and a residue of boric oxide (1·72 g., 93%).

(b) *The 3-isomer.* Tri-3-methylallyl borate (8·56 g., >2 mols.) was added to boron trichloride (1·39 g., 1 mol.) at −80°, the reaction being vigorous. After 20 hr. at 20°/15 mm., a condensate of butenyl chloride (2·38 g., 74%), n_D^{20} 1·4281 (Found: Cl, 39·0%), had collected in a trap at −80°. The remainder afforded tri-3-methylallyl borate (5·90 g., 100%), b. p. 126°/15 mm., n_D^{20} 1·4431, and a residue of boric oxide.

Stability of the But-3-enyloxyboron Chlorides.—In order to ascertain the stability at 20° of the but-3-enyloxyboron chlorides with respect to reactions (8) and (9), samples (*ca.* 0·20 g.) of the compounds, prepared as above, were withdrawn and sealed off. These were analysed after stated times for easily hydrolysable chlorine and boron; the change in the ratio of the two estimations enables the percentage decompositions to be calculated. Di-3-butenyl chloroboronate was substantially unchanged (<1% decomp.) after 22 hr. But-3-enyl dichloroboronate was 11% decomposed after 3 hr., and 92% decomposed after 21 hr.

Interaction between Bis-3-methylallyl Ether and Boron Trichloride [Reaction (10)].—The ether (8·07 g., 3 mols.) was added, with stirring, to the trichloride (5·00 g., 2 mols.) at −80°. A red-orange lower layer formed. The mixture was kept at 20°/10 mm. for 3½ hr. Butenyl chloride (7·60 g., 66%), n_D^{22} 1·4271 (Found: Cl, 39·3%), was collected at −80° and a residue containing boric oxide (1·47 g., 97%) remained in the reaction vessel.

Effect of Boron Trichloride on 3-Methylallyl Chloride.—The trichloride (0·05 g.) was added to 3-methylallyl chloride (6·67 g.), n_D^{20} 1·4346, at −80°. The mixture was allowed to remain at 20° for 1 hr., whereafter it was washed with water and dried ($MgSO_4$). Unchanged 3-methylallyl chloride, n_D^{20} 1·4346, was obtained.

When boron trichloride (1·10 g.) at −80° was added to 3-methylallyl chloride (5·92 g.) at −80° and the mixture allowed to warm to room temperature in series with a trap at −80°, a

yellow liquid was obtained, which rapidly darkened and after 1 hr. had become a brown gum. Removal of volatile matter at 10 mm. afforded boron trichloride and a residue (5·92 g.). This was soluble in acetone, benzene, carbon tetrachloride, and ethanol, but insoluble in water. An iodine value (Wijs's method) suggested that the material has a molecular weight of 1448.

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THE NORTHERN POLYTECHNIC,
HOLLOWAY ROAD, LONDON, N.7. [*Received, November 7th*, 1956.]

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313. *Synthetic Applications of Activated Metal Catalysts. Part III.* Desulphurisation of Thiazoles with Raney Nickel.*

By G. M. BADGER and N. KOWANKO.

Benzothiazoles are desulphurised, in excellent yield, to the expected secondary amines by treatment with very active Raney nickel (W6 or W7) in boiling methanol. Neutral, less active catalysts (W5) are relatively ineffective; but in the presence of alkali, ring fission followed by desulphurisation occurs to yield mixtures of aniline, methylaniline, and *o*-aminothiophenol.

Simple substituted thiazoles are more labile and desulphurisation apparently occurs by two competing mechanisms. In the first (favoured by alkaline conditions) ring fission evidently occurs before desulphurisation. In the second (favoured by the use of the neutral W6 catalyst) the initial desulphurisation is followed by fission of a C–N bond and formation of carbonyl derivatives by hydrolysis.

DESULPHURISATION of thiophen derivatives with Raney nickel has been extensively investigated in recent years, and has been used for the preparation of a wide variety of fatty acids.[1,2] However, relatively few attempts to desulphurise thiazoles have been recorded, and indeed the literature is discouraging. Thus Cook, Heilbron, and Levy[3] removed only the mercapto-group by treatment of 5-amino-2-mercapto-4-phenylthiazole with Raney nickel. Similarly 2-mercaptobenzothiazole has been converted into benzothiazole[4] with catalyst prepared by the Mozingo method;[5] but under alkaline conditions a mixture of aniline and methylaniline was reported.[4] Hurd and Rudner[6] obtained *o*-aminothiophenol, *o*-aminodiphenyl disulphide, and aniline on desulphurisation of benzothiazole in the presence of ammonia. A systematic examination of the desulphurisation of thiazoles and benzothiazoles is now reported.

The mechanism of the desulphurisation is still obscure, but it is reasonable to assume that the initial step involves chemisorption of the sulphur on the catalyst by means of the sulphur's lone-pair of electrons. No complicating factors exist with simple thiophen derivatives, but with thiazoles the lone pair of the hetero-nitrogen atom will compete for the active centres in much the same way that pyridine and other similar heteroaromatic compounds act as catalyst "poisons" in hydrogenations.[7,8] That is presumably why thiazoles are more difficult to desulphurise than thiophen derivatives. So most of the present work was carried out with the very active (neutral) W6 and the similarly active

* Part II, *J.*, 1956, 616.

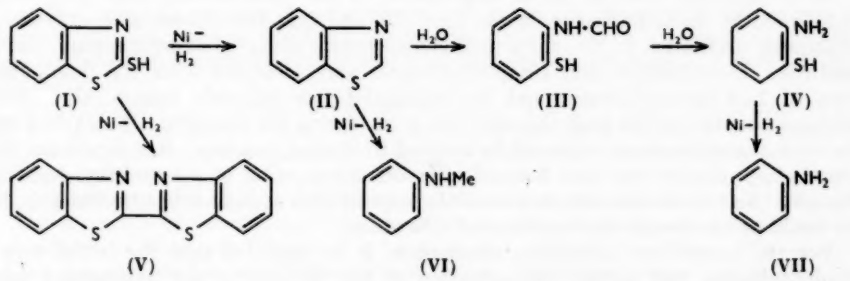
[1] Badger, Rodda, and Sasse, *J.*, 1954, 4162.
[2] Sy, Buu-Hoï, and Dat Xuong, *Compt. rend.*, 1954, **239**, 1224, 1813; 1955, **240**, 442, 785; *Bull. Soc. chim. France*, 1955, 1583; Sy, *ibid.*, p. 1175.
[3] Cook, Heilbron, and Levy, *J.*, 1947, 1598.
[4] Ivanoff and Ivanoff, *Compt. rend. Acad. bulgare Sci.*, 1952, **5**, No. 1, 13.
[5] Mozingo, Wolf, Harris, and Folkers, *J. Amer. Chem. Soc.*, 1943, **65**, 1013; Mozingo, *Org. Synth.*, 1941, **21**, 15.
[6] Hurd and Rudner, *J. Amer. Chem. Soc.*, 1951, **73**, 5157.
[7] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 456; Elsner and Paul, *J.*, 1953, 3156.
[8] Badger and Sasse, *J.*, 1956, 616.

(alkaline) W7 catalysts.[9] The solvent is also important in desulphurisations and for non-acidic sulphur compounds ethanol has been most commonly used. However, as primary amines had been reported among the products of some thiazole desulphurisations,[4,6] and as ethanol is known to ethylate such bases in the presence of Raney nickel,[10] this solvent seemed contraindicated. Methanol was therefore used for most of the experiments as this alcohol does not alkylate amines in the presence of Raney nickel.

When treated with either W6 or W7 catalyst in boiling methanol both benzothiazole (II) and 2-methylbenzothiazole were smoothly desulphurised in excellent yield to the expected methylaniline and ethylaniline respectively. W5 catalyst was less effective, however, for with 2-mercaptobenzothiazole (I) it gave only benzothiazole (II) and a trace of 2 : 2′-dibenzothiazolyl (V). The latter was presumably formed by dimerisation of two free radicals resulting after removal of the thiol groups.

With W5 in methanol to which sodium hydroxide had been added, 2-mercaptobenzothiazole gave a mixture of aniline, methylaniline, *o*-aminodiphenyl disulphide, and dibenzothiazolyl. In a related experiment in which benzothiazole was refluxed with alkaline methanol before addition of W5 catalyst, the proportion of aniline to methylaniline was greatly increased. Similarly, reaction of 2-mercaptobenzothiazole with a W7 catalyst which had been heated *in vacuo* to remove some of the hydrogen (" dehydro-W7 ") gave aniline, methylaniline, benzothiazole, and dibenzothiazolyl.

The thiazole ring is known to be subject to ring fission in the presence of alkali. With the very active (alkaline) W7 catalyst it seems that desulphurisation occurs before ring fission, and the secondary amine is the only product. With the less active W5 and dehydro-W7 catalyst, however, it seems that ring fission occurs to some extent before



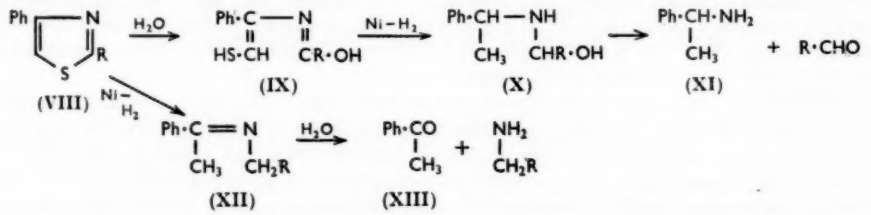
desulphurisation. The intermediate formyl derivative (III) would then give *o*-aminothiophenol (IV) and this was isolated in its oxidised form, 2 : 2′-diaminodiphenyl disulphide. The isolation of this product was only made possible by the use of less than the optimum amount of nickel catalyst; but desulphurisation did occur to some extent, giving aniline (VII).

Desulphurisation of several 4-phenylthiazoles and of 2-amino-4-methyl-5-phenylthiazole with either W6 or W7 catalyst has been found to be more complex. All the 4-phenylthiazoles (VIII) gave α-methylbenzylamine (XI) with either catalyst, and 2-amino-4-methyl-5-phenylthiazole gave the analogous product, α-methylphenethylamine, showing that cleavage of the $C_{(2)}$–N bond had taken place as well as hydrogenolysis of the C–S bonds. The 2-aminothiazoles all evolved ammonia vigorously. With W6 catalyst 4-phenylthiazole and 2-amino-4-phenylthiazole both gave some acetophenone (XIII); but this

[9] Billica and Adkins, *Org. Synth.*, 1949, **29**, 24; Adkins and Billica, *J. Amer. Chem. Soc.*, 1948, **70**, 695.

[10] Rise and Kohn, *ibid.*, 1955, **77**, 4052; Kao, Tilak, and Venkataraman, *J. Sci. Ind. Res., India*, 1955, **14**, *B*, 624.

compound was not detected when W7 was used. However, 2-amino-4-methyl-5-phenylthiazole gave the analogous phenylacetone with both W6 and W7, and 2-α-naphthyl-4-phenylthiazole also gave some acetophenone with W7. No ketone was isolated after reaction of 2 : 4-diphenylthiazole with either catalyst, and on distillation of the basic fraction disproportionation took place to give α-methylbenzylamine (XI) and benzaldehyde. A similar disproportionation occurred when the basic fraction from the desulphurisation of 2-α-naphthyl-4-phenylthiazole was heated, and α-methylbenzylamine and 1-naphthaldehyde were isolated. Some 1-methylnaphthalene was also detected after desulphurisation of this thiazole.



The most reasonable explanation for these results is that two competing mechanisms are operating, the extent of each depending on the experimental conditions and particularly on the alkalinity of the mixture. W7 catalyst contains a considerable amount of caustic alkali and this may well lead to ring fission of the thiazole system before desulphurisation : however, the mixture is alkaline even when W6 is used on account of the presence of the thiazole itself and (as the reaction proceeds) of the basic products.

It is suggested that an initial ring fission to the intermediate thiol (IX) would be followed by desulphurisation to the base (X), and that this disproportionates during subsequent distillation to give the α-methylbenzylamine observed experimentally, and an aldehyde. Benzaldehyde and 1-naphthaldehyde were identified after the desulphurisation of 2 : 4-diphenylthiazole and 2-α-naphthyl-4-phenylthiazole respectively. Some disproportionation of the base (X) may also occur during the reaction. If this does take place the aldehyde concerned would be reduced to the hydrocarbon : it is significant that 1-methylnaphthalene was also isolated after desulphurisation of 2-α-naphthyl-4-phenylthiazole. No toluene was detected in similar experiments with 2 : 4-diphenylthiazole, but this could well be due to the experimental difficulties.

For the second and competing mechanism, it is suggested that the initial step is desulphurisation and partial hydrogenation of the thiazole to the unsaturated intermediate (XII). Fission of this with acid, during working-up, would give acetophenone (XIII), and this product has been isolated in nearly all experiments involving desulphurisation with W6 catalyst. Similarly, desulphurisation of 2-amino-4-methyl-5-phenylthiazole with either W6 or W7 gave some of the analogous phenylacetone. Moreover, Hurd and Rudner [6] also isolated acetophenone on desulphurisation of both 2-mercapto- and 2-amino-4-phenylthiazole. Such a mechanism implies the formation of a primary amine ($R{\cdot}CH_2{\cdot}NH_2$) as the second fragment. No methylamine could be detected during the actual desulphurisation of 4-phenylthiazole; but methylamine was evolved and identified on treatment of the reaction mixture with hydrochloric acid. It seems therefore that hydrogenolysis stops at the intermediate (XII), and that fission to the ketone (XIII) and the primary amine is a hydrolytic process catalysed by hydrochloric acid.

Experimental

Preparation of Catalysts.—The Raney nickel catalysts designated W5, W6, and W7 were prepared by the methods of Billica and Adkins [9] except that for the final washings methanol was used in place of ethanol, and the centrifugation was omitted. The catalyst was freshly

prepared for each experiment. " Dehydro-W7 " catalyst was prepared as described by Badger and Sasse.[8]

Desulphurisation of 2-Mercaptobenzothiazole.—(i) A mixture of 2-mercaptobenzothiazole (10 g.), W5 Raney nickel (from 65 g. of alloy), and methanol (250 c.c.) was refluxed for 8 hr. The hot mixture was filtered, the catalyst was washed with boiling methanol, and the combined filtrates were evaporated. An additional small amount of product was obtained on dissolution of the catalyst in dilute hydrochloric acid, basification, steam-distillation, and extraction of the distillate with ether. The combined oil was distilled, to give benzothiazole, b. p. 230° (4·41 g., 54·5%). The picrate formed yellow needles, m. p. and mixed m. p. 169·5—170° (Found : C, 43·2; H, 2·5; N, 15·5. Calc. for $C_{13}H_8O_7N_4S$: C, 42·9; H, 2·2; N, 15·4%). The residue from the distillation was recrystallised from xylene. 2 : 2′-Dibenzothiazolyl (10 mg.) formed plates, m. p. 297·5—298° alone or mixed with a specimen prepared by the method of Zubarowski [11], who, however, gives m. p. 306—308°.

(ii) In a similar experiment, sodium hydroxide (2 g.) was added to the reaction mixture. Evaporation of the methanol gave a tarry residue which was dissolved in ether and extracted with dilute sodium hydroxide. When kept in air the alkaline extract deposited 2 : 2′-diaminodiphenyl disulphide (0·75 g., 10·1%) as yellow plates, m. p. and mixed m. p. 93—94° (Found : C, 58·0; H, 4·7; N, 11·4; S, 26·4. Calc. for $C_{12}H_{12}N_2S_2$: C, 58·1; H, 4·8; N, 11·3; S, 25·8%). The dihydrochloride of this base crystallised from concentrated hydrochloric acid as needles, m. p. 210—211° (Found : C, 40·3; H, 5·2. Calc. for $C_{12}H_{18}O_2N_2S_2Cl_2$: C, 40·5; H, 5·1%). The recorded m. p.[12] for this salt (112—114°) seems to be in error.

The oil obtained by evaporation of the ether was subjected to a Hinsberg separation with toluene-*p*-sulphonyl chloride (9 g.) and 10% aqueous sodium hydroxide. This gave 2 : 2′-dibenzothiazolyl (0·55 g., 6·9%), *N*-methyltoluene-*p*-sulphonanilide (4·1 g., 47·5%), and toluene-*p*-sulphonanilide (1·5 g., 16·5%), all identified by comparison with authentic specimens.

(iii) 2-Mercaptobenzothiazole (12 g.) in methanol (150 c.c.) was refluxed with dehydro-W7 nickel (from 125 g. of alloy) for 29 hr. Extraction of the catalyst with methanol and xylene and concentration to small volume gave 2 : 2′-dibenzothiazolyl (0·52 g., 5·6%), m. p. and mixed m. p. 295—298°. The residual oil, on treatment with toluene-*p*-sulphonyl chloride and aqueous sodium hydroxide, gave benzothiazole, b. p. 230° (3·44 g., 35·1%) (picrate, m. p. 169°), *N*-methyltoluene-*p*-sulphonanilide (3·60 g., 22%), and toluene-*p*-sulphonanilide (1·23 g., 7·2%), identified as above.

Desulphurisation of Benzothiazole.—(i) Benzothiazole (6 g.), W7 Raney nickel (from 65 g. of alloy), and methanol (250 c.c.) were refluxed for 3 hr. Treatment of the product with toluene-*p*-sulphonyl chloride and sodium hydroxide gave *N*-methyltoluene-*p*-sulphonanilide (8·4 g., 84%) as sole product.

(ii) Similar desulphurisation with W6 Raney nickel, etc., gave the same amide in 87% yield.

(iii) A mixture of benzothiazole (10 g.) and sodium hydroxide (15 g.) in methanol (150 c.c.) was refluxed for 2½ hr., and W5 Raney nickel (from 65 g. of alloy) then added. After a further 8 hours' refluxing the product was treated with toluene-*p*-sulphonyl chloride to give *N*-methyltoluene-*p*-sulphonanilide (1·23 g., 7·25%) and toluene-*p*-sulphonanilide (4·69 g., 29·5%).

(iv) Benzothiazole (10 g.) and dehydro-W7 Raney nickel (from 65 g. of alloy) in sulphur-free xylene (35 c.c.) were refluxed for 12 hr. (cf. ref. 8). Distillation of the product gave unchanged benzothiazole (8·4 g.) and the residue, after recrystallisation from xylene, was identified as 2 : 2′-dibenzothiazolyl (0·02 g.) as usual.

Desulphurisation of 2-Methylbenzothiazole.—(i) 2-Methylbenzothiazole (5 g.), W6 Raney nickel (from 65 g. of alloy), and methanol (250 c.c.) were refluxed for 3 hr. The product gave *N*-ethyltoluene-*p*-sulphonanilide (8·35 g., 82%) as needles, m. p. and mixed m. p. 86°.

(ii) Similar desulphurisation with W7 Raney nickel gave the amide in 80% yield. No by-products could be detected in either case.

Preparation of Thiazoles.—4-Phenylthiazole [13] was prepared from phenacyl bromide and thioformamide; 2 : 4-diphenylthiazole [14] from phenacyl bromide and thiobenzamide; and 2-amino-4-phenylthiazole [15] from phenacyl bromide and thiourea.

[11] Zubarowski, *Zhur. obshchei Khim.*, 1951, **21**, 2055.
[12] Cymerman-Craig, Rogers, and Warwick, *Austral. J. Chem.*, 1955, **8**, 252.
[13] Wiley, England, and Behr, " Organic Reactions," 1951, Vol. VI, 367.
[14] Hubacher, *Annalen*, 1890, **259**, 237.
[15] Traumann, *ibid.*, 1888, **249**, 35.

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2-α-*Naphthyl*-4-*phenylthiazole*. A solution of α-naphthonitrile (30 g.) and dimethylamine (2 c.c.) in ethanol (200 c.c.) was cooled to −10° and saturated with hydrogen sulphide, quickly transferred to an autoclave, and heated at 80—90° for 4 hr. After evaporation the residue was extracted with ether, and the extract washed with dilute hydrochloric acid and water, dried, and evaporated. The resulting crude α-thionaphthamide (9 g.) was heated with phenacyl bromide (9·6 g.), sodium acetate (3·85 g.), and ethanol (45 c.c.) on the steam-bath until the solvent had evaporated. Water was added, the mixture extracted with ether, and the ether dried and evaporated. After chromatography in light petroleum, on alumina, and crystallisation from light petroleum, **2-α-*naphthyl*-4-*phenylthiazole*** (11·0 g., 19·5%) formed plates, m. p. 88° (Found: C, 79·5; H, 4·5; N, 4·5. $C_{19}H_{13}NS$ requires C, 79·4; H, 4·5; N, 4·9%).

2-*Amino*-4-*methyl*-5-*phenylthiazole*. Benzyl methyl ketone [16] (70 g.), thiourea (78 g.), and iodine (133 g.) were heated on the steam-bath for 8 hr.[17] The mixture was then extracted with ether, and the residue dissolved in boiling water and treated with charcoal. The filtrate was basified with potassium carbonate, and the product purified by recrystallisation from ethanol and then benzene. **2-*Amino*-4-*methyl*-5-*phenylthiazole*** (21 g., 21%) was obtained as plates, m. p. 165° (Found: C, 63·4; H, 5·2. $C_{10}H_{10}N_2S$ requires C, 63·2; H, 5·3%). The *picrate* crystallised from ethanol in yellow needles, m. p. 248° (Found: C, 45·9; H, 3·2; N, 16·5. $C_{16}H_{13}O_7N_5S$ requires C, 45·8; H, 3·1; N, 16·7%).

Desulphurisation of **4-*Phenylthiazole***.—(i) 4-Phenylthiazole (10 g.), W7 Raney nickel (from 65 g. of alloy), and methanol (250 c.c.) were refluxed for 3 hr. The combined filtrate and methanol washings were acidified with dilute hydrochloric acid (100 c.c.), and the solvent was evaporated on the steam-bath. Basification of the dark red residue with 20% aqueous sodium hydroxide, followed by ether-extraction and distillation of the dried extracts, gave α-methylbenzylamine, b. p. 190—195° (2·3 g.), characterised as the oxalate, m. p. 235—236° (lit., m. p. 238°) (Found: C, 65·0; H, 7·2; N, 8·2. Calc. for $C_{18}H_{24}O_4N_2$: C, 65·1; H, 7·2; N, 8·4%). A higher-boiling fraction (1·3 g.) was identified as unchanged 4-phenylthiazole (m. p. 44°) (picrate, m. p. and mixed m. p. 163°).

(ii) Similar desulphurisation with W6 Raney nickel and evaporation of the acidified solvent gave a dark red residue. Extraction with ether and water, and subsequent evaporation of the dried ethereal solution, gave acetophenone (0·75 g.), identified as the 2 : 4-dinitrophenylhydrazone. The aqueous extract was basified and warmed, the liberated methylamine being identified by passing the gas into a solution of 1-chloro-2 : 4-dinitrobenzene. The cooled alkaline solution was then extracted with ether and evaporation of the dried solution gave the basic products. Distillation gave α-methylbenzylamine, b. p. 195° (1·95 g.) (oxalate, m. p. and mixed m. p. 235°), and 4-phenylthiazole (1·55 g.), identified as the picrate.

Desulphurisation of **2-*Amino*-4-*phenylthiazole***.—(i) Desulphurisation of 2-amino-4-phenylthiazole (10 g.) with W7 catalyst as described for 4-phenylthiazole gave α-methylbenzylamine (4·03 g.) {oxalate, m. p. and mixed m. p. 235°; chloroplatinate, m. p. 215—216° (decomp.) [lit., m. p. 213—214° (decomp.)]}. Ammonia was liberated during the reaction, and a very little methylamine was also detected by using 1-chloro-2 : 4-dinitrobenzene.

(ii) Similar desulphurisation by means of the W6 catalyst and subsequent evaporation of the acidified methanol gave a partly solid mass, which was filtered off and washed with ether. Recrystallisation of the solid from dilute hydrochloric acid gave 2-amino-4-phenylthiazole hydrochloride (4 g.), m. p. and mixed m. p. 204°. The ethereal solution, which was separated into neutral and basic fractions, gave acetophenone (1·50 g.), identified as the 2 : 4-dinitrophenylhydrazone, and α-methylbenzylamine (2·15 g.; b. p. 190°) identified as the oxalate, m. p. and mixed m. p. 235°.

Desulphurisation of **2 : 4-*Diphenylthiazole***.—(i) Desulphurisation of 2 : 4-diphenylthiazole (10 g.) with W7 Raney nickel as described for 4-phenylthiazole gave benzaldehyde (1·65 g., 28%), identified as the 2 : 4-dinitrophenylhydrazone, and α-methylbenzylamine (1·05 g., 18·6%), identified as the oxalate, m. p. 235°.

(ii) Similar desulphurisation by means of W6 Raney nickel gave a product which was separated into basic and non-basic fractions. Recrystallisation of the " non-basic " fraction from benzene–hexane gave unchanged 2 : 4-diphenylthiazole (2·35 g.), identified by comparison with an authentic specimen. The basic fraction was distilled, to give α-methylbenzylamine (b. p. 195°; 0·95 g.) identified as the oxalate, m. p. 235°, and another fraction which

[16] *Org. Synth.*, Coll. Vol. II, p. 391.
[17] Cf. King and Hlavecek, *J. Amer. Chem. Soc.*, 1950, **72**, 3722.

decomposed at *ca.* 250° with evolution of ammonia. From this fraction benzaldehyde (2·53 g.) was obtained as the 2 : 4-dinitrophenylhydrazone.

Desulphurisation of 2-Amino-4-methyl-5-phenylthiazole.—(i) Desulphurisation of this thiazole (8 g.) was effected as usual with W7 catalyst, and the residue, after evaporation of the acidified solvent, separated into neutral and basic fractions. The neutral fraction (0·25 g.) was identified as phenylacetone, giving a 2 : 4-dinitrophenylhydrazone, orange needles, m. p. 155° (lit., m. p. 155—156°), and a semicarbazone, needles, m. p. 195° (lit., m. p. 195—198°). Distillation of the basic fraction gave α-methylphenethylamine (1·175 g.; b. p. 200—202°) (lit., b. p. 203°) (Found : C, 80·25; H, 9·95; N, 10·2. Calc. for $C_9H_{13}N$: C, 80·0; H, 9·6; N, 10·4%). The chloroplatinate crystallised from dilute hydrochloric acid in golden-yellow needles, decomp. *ca.* 220°. The analytical specimen was dried *in vacuo* over sodium hydroxide and phosphoric oxide (Found : C, 31·9; H, 4·4; N, 4·05; Cl, 30·7; Residue, 27·9. Calc. for $C_{18}H_{28}N_2Cl_6Pt$: C, 31·8; H, 4·1; N, 4·1; Cl, 31·3; Pt, 28·7%). Distillation of the high-boiling fraction gave unchanged 2-amino-4-methyl-5-phenylthiazole (0·85 g.) identified as the picrate, m. p. and mixed m. p. 248°.

(ii) Similar desulphurisation over W6 catalyst gave a partly solid product. Separation of the crystals, followed by basification, gave unchanged 2-amino-4-methyl-5-phenylthiazole (2·77 g.), identified as the picrate. The liquid product was separated into neutral and basic fractions. The neutral fraction (0·75 g.) was identified as phenylacetone, giving a 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 155°. Distillation of the basic fraction gave α-methylphenethylamine (b. p. 200—203°; 1·80 g.), identified as the chloroplatinate. Recrystallistion of the residue gave unchanged base (2·55 g.), identified as the picrate.

Desulphurisation of 2-α-Naphthyl-4-phenylthiazole.—Desulphurisation of the thiazole (10 g.) was effected by 3 hours' refluxing with W7 Raney nickel (from 65 g. of alloy) in methanol (250 c.c.). The combined filtrate and washings was acidified with dilute hydrochloric acid (100 c.c.) and evaporated. Addition of excess of picric acid to the distillate, followed by concentration, gave 1-methylnaphthalene picrate (1·8 g.). After recrystallisation from ethanol this had m. p. and mixed m. p. 142°. The residue from the desulphurisation was separated into basic and non-basic fractions in the usual way. The latter, on removal of the ether, deposited unchanged base (2·15 g.), identified by comparison with an authentic specimen. Distillation of the remainder of the neutral fraction gave acetophenone (0·38 g.), identified as the dinitrophenylhydrazone. The basic fraction gave α-methylbenzylamine (0·85 g.; identified as the oxalate, m. p. 235°), and distillation of the high-boiling fraction (b. p. 260—280°) gave a yellow oil (2·05 g.). The major portion (2·0 g.) was shown to be 1-naphthaldehyde by conversion into its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 255°.

Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne. We are also grateful to Dr. W. H. F. Sasse for helpful discussions.

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, November 13th,* 1956.]

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314. *The Intensities of the Forbidden Bands of Benzene.*

By (Mrs.) J. K. Thompson and A. D. E. Pullin.

The peak densities of the 1174 cm.$^{-1}$ forbidden band and the peak densities and half-intensity widths of the 851 cm.$^{-1}$ forbidden band of benzene have been measured for solutions of benzene in a variety of solvents. It was found that the peak densities increased smoothly and rapidly with increase of the refractive index of the solvent. The peak density for the carbon disulphide solution was anomalously large. A similar trend was found for the peak densities of the allowed 1033 cm.$^{-1}$ band and could be explained on the basis of decreasing half-intensity width of this band with increasing solvent refractive index. The product of the peak density and half-intensity width of the 851 cm.$^{-1}$ band was taken as a proportionate measure of the area of this band. The product was found to increase with increasing solvent polarisability and decreasing solvent molar volume. Carbon disulphide solution gave the highest value of this product. It is suggested that the large half-intensity widths of the forbidden bands are due to the fact that the transition moment for transitions giving rise to absorption at the wings of the bands is larger than that for transitions giving rise to absorption at frequencies near the band maximum.

It is well known that liquid benzene and solutions of benzene show a number of weak absorption bands at frequencies corresponding to fundamental modes of vibration which are forbidden to be active in absorption by the selection rules for D_{6h} symmetry. Bands at these frequencies might conceivably arise from combination tones or be due to benzene molecules whose mass symmetry is lowered by the presence of ^{13}C. However, considerations of likely allowed combination tones and the comparison made by Halford and Schaefer [1] of the spectra of the liquid and vapour [2] for equivalent absorbing paths rule out both these interpretations, at least as an explanation of the major part of the intensity of these bands. Thus at least nearly all the intensity of these bands must be due to forbidden fundamental vibrations rendered active through the disturbance of the molecule by intermolecular forces.

Following Mair and Hornig's assignment [3] for the two B_{2u} vibrational modes and that of Ingold *et al.*[4] for the remainder, the most prominent of the forbidden bands are: (*a*) A band at 851 cm.$^{-1}$ * corresponding to the E_g^- out-of-plane hydrogen bending mode.[5] (*b*) A band at 1175 cm.$^{-1}$ partly overlapped by a weaker band at 1148 cm.$^{-1}$ corresponding respectively to the E_g^+ and the B_{2u} in-plane hydrogen bending modes.

In an attempt to find what solvent properties are important in causing these forbidden bands to appear, we have examined the spectra of a variety of solutions of benzene. The peak densities, and in some cases the half-intensity widths, have been measured for both forbidden and allowed bands, and a dependence of these quantities on the refractive index of the solvent has been established.

Experimental

All the spectra were obtained with a Perkin-Elmer model 21 double-beam spectrophotometer equipped with a sodium chloride prism. Useful solution spectra were obtained with the following solvents: methyl cyanide (1), *n*-hexane (2), ethylidene chloride (3), methylene

* Frequencies quoted are those for liquid benzene: corresponding frequencies for the solutions varied slightly with solvent (Fig. 2).

[1] Halford and Schaefer, *J. Chem. Phys.*, 1946, **14**, 141.

[2] A spectrum of liquid benzene obtained at higher resolution than that of Ref. 1. is given in Ref. 3, p. 1239. Liquid and vapour spectra are reproduced by Ingold (*J.*, 1936, 935) and by the American Petroleum Institute Research Project 44, spectra 122 (vapour), 307 and 498 (liquid).

[3] Mair and Hornig, *J. Chem. Phys.*, 1949, **17**, 1236.

[4] Ingold *et al.*, *J.*, 1946, 222 *et seq.*, especially p. 325.

[5] *Idem, ibid.*, p. 231.

chloride (4), *cyclo*hexane (5), *n*-tetradecane (6), carbon tetrachloride (7), phosphorus oxychloride (8), trichloroethylene (9), benzene (10), methylene bromide (11), bromoform (12), carbon disulphide (13), sulphur monochloride (14), methylene iodide (15). The grades or sources of these chemicals were: (7) and (13), " AnalaR "; (1), May and Baker Laboratory Chemicals; (9), Technical: the remainder, B.D.H. Laboratory Reagent. The solvents were used without further purification, except for (14) which was distilled before use. The benzene used was of " AnalaR " quality: preliminary experiments showed that its spectrum remained unchanged when the benzene was subjected to repeated recrystallisation. All solutions of benzene except those in phosphorus oxychloride and sulphur monochloride were made up by volume to 0·8 volume fraction of solvent by adding benzene to 8 ml. of solvent to give a final volume of 10 ml. The weights of the solvent and benzene were noted.

For measurements of the forbidden bands the following procedure was adopted. Spectra compensated for solvent absorption were obtained with the solution and solvent in Hilger variable-path cells set at 0·200 and 0·160 mm., respectively. By making up the solutions on the basis of a constant volume of solvent one setting of the variable-path cells could be used throughout and only small corrections needed to be made to the observed intensities to refer them to a constant weight (taken as 1·76 g.) of benzene in 10 ml. of solution. For solutions in phosphorus oxychloride and sulphur monochloride a similar procedure was followed except that a solvent volume fraction of 0·714 was used in conjunction with fixed-thickness cells of 0·140 and 0·100 mm. Comparison spectra of pure benzene were obtained in two ways: first by obtaining a " solvent-compensated " spectrum with the variable-path cells both filled with pure benzene; and, secondly, with a single variable-path cell set at 0·040 mm. For all the solvents employed the spectrum of the compensating cell alone filled with the solvent was obtained. Spectral regions of the solution, solvent-compensated spectrum in which the solvent absorption exceeded 50% were not further considered.*

Because of the dependence on medium of the frequency, shape, and intensity of solvent absorption bands, the bands of the solvent are modified by the presence of the benzene in the solution, so that, apart from volumetric inaccuracies, compensation of solvent absorption cannot be quite exact. (A shift of solvent band position shows up on the solvent-compensated solution spectrum as sharp twinned upward and downward peaks like an anomalous dispersion curve: this effect was most noticeable in the spectra of solutions in bromoform, carbon disulphide, and methylene iodide.) To avoid errors arising from inexact solvent compensation, solute peak intensities were measured only if the solvent absorption at the solute band peak was less than 30% and remained less than 50% for a distance of 20 cm.$^{-1}$ on either side.

Further errors arise from the estimation of the base line for zero benzene absorption. This was estimated from regions of the spectrum between 4000 and 2000 cm.$^{-1}$ which were free from absorption bands due to either solvent or benzene. Other procedures, such as assigning a suitable small constant value to the optical density at the minimum of absorption on the low-frequency side of the 1970 cm.$^{-1}$ benzene band would have given essentially the same results. To allow for these and other errors, lines are drawn through the points in Figs. 4 and 5, representing, in optical density units, $\pm$(0·003 plus 5% of the solvent optical density at that frequency).

Because both the 851 and the 1174—1148 cm.$^{-1}$ band are considerably overlapped by the wings of neighbouring bands it is not possible to measure the band areas accurately. Where possible, approximate half-intensity widths have been measured and in these cases the product of half-intensity width and peak density ($\log_{10} I_0/I$) has been used as a proportionate measure of band area. Because of the width of forbidden bands, no correction for finite slit width need be applied. To check that large concentration errors were not occurring, the band areas of the 1819 and the 1970 cm.$^{-1}$ combination bands were measured approximately from the same spectra as the forbidden bands. The former remained within $\pm$10% of a mean value for all the solvents employed; a variation probably mainly arising from errors in measuring the half band widths. The constancy of the spacing of the variable path cells was checked obtaining the interference spectra of the empty cells.

Measurements of the peak densities and half-intensity widths of the allowed benzene band at 1033 cm.$^{-1}$ were also made for solutions of benzene in a number of the solvents listed above. (The 1033 cm.$^{-1}$ band arises from an in-plane E_u^- hydrogen bending mode.[5]) For these measurements solutions of the same concentration as before were used, but owing to the greater intensity

* The spectrum of pure benzene obtained by the first method was an exception to this.

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of this band the variable-path cells were set at 0·040 and 0·032 mm. The products of the half-intensity band width and peak density were found to vary by less than 10% from a mean value for the solvents used.

Results

The band areas or integrated intensities of the 851 cm.$^{-1}$ band and the 1174—1148 cm.$^{-1}$ pair in different solvents should be used as a measure of the perturbing power of the different

Fig. 1. *Benzene spectra for equivalent absorbing paths:* 1450—750 *cm.*$^{-1}$. *A, Liquid benzene,* 0·040 *mm. layer. B, Carbon disulphide solution of benzene. C, Methylene iodide solution of benzene. Spectra B and C are successively displaced downward; the horizontal lines represent* 100% *transmission for spectra B and C.*

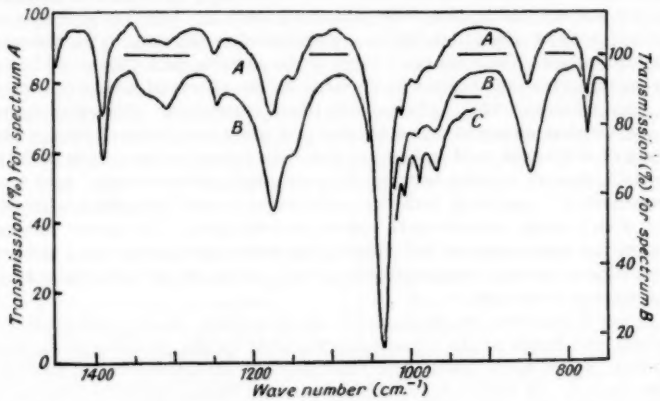


Fig. 2. *Benzene solution spectra for equivalent absorbing paths:* 900—750 *cm.*$^{-1}$. *The solvents are: A,* n*-tetradecane; B, methylene bromide; C, methylene iodide; D, carbon disulphide. Vertical lines represent* 10% *absorption.*

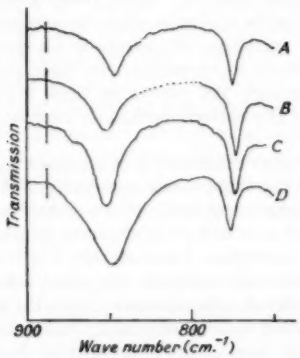
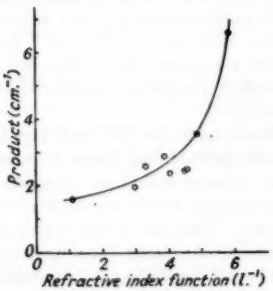


Fig. 3. *Plot of the product of peak density and half-intensity band width for the* 851 *cm.*$^{-1}$ *band against the solvent function* $(n^2 - 1)/(n^2 + 2)V$. *In increasing value of the abscissae, the points are for the solvents* 6, 3, 10, 12, 1, 11, 14, 15, 13.



solvents. However, because of the width of the forbidden bands and consequent overlapping with neighbouring more intense bands, direct measurement of their band areas is difficult. For cases where reliable half-intensity widths could be obtained the product of half-intensity width and peak density has been taken as an approximately proportional measure of band area. Half-intensity widths of the forbidden bands definitely varied with the solvent, though precise measurement was difficult. In order of increasing half-intensity width the solvents were;

n-tetradecane, sulphur monochloride, and methylene iodide, 19 cm.$^{-1}$; bromoform, 22 cm.$^{-1}$; methylene bromide 24 cm.$^{-1}$; ethylidene chloride, 25 cm.$^{-1}$; benzene, 28 cm.$^{-1}$; carbon disulphide, 33 cm.$^{-1}$; methyl cyanide, 35 cm.$^{-1}$. These are probably correct to ± 2 cm.$^{-1}$. Half-intensity widths of the 1819 and 1970 cm.$^{-1}$ allowed combination bands show a similar solvent order, except in carbon disulphide solution, in which these bands are among the narrowest. The experimental findings may be summarised as follows:

(*a*) Even excluding the carbon disulphide solution of benzene, there appears to be a much greater dependence of the integrated intensities of the 851 cm.$^{-1}$ band than is found for the 1033 cm.$^{-1}$ band, or for allowed bands generally (Figs. 1 and 2).

(*b*) The forbidden bands are symmetrical but much broader than the allowed bands. [Compare the allowed combination bands at 774, 1250, and 1394 cm.$^{-1}$ with the forbidden fundamental bands at 851 and 1174 cm.$^{-1}$ (Fig. 1).]

(*c*) The present rather limited results suggest that the integrated intensities of the forbidden bands increase fairly steeply with some function of the solvent refractive index n and solvent molar volume V, such as $n/V^{1/3}$ or $(n^2 - 1)/(n^2 + 2)V$ (Fig. 3) (n_α^{20} values have been used throughout).

FIG. 4. *Plot of peak densities against solvent refractive index for the 851 cm.$^{-1}$ band. Solvents, in order of increasing refractive index, are:* 1—4, 6, 8, 10—15.

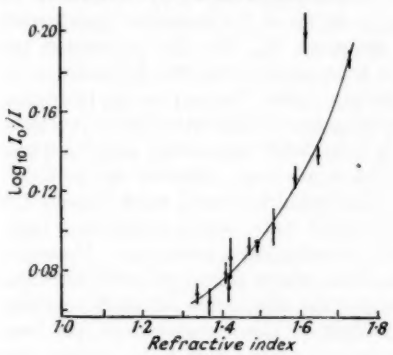
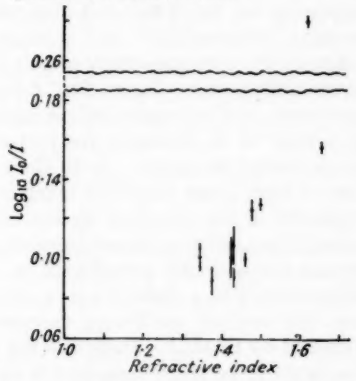


FIG. 5. *Variation of peak density of 1174 cm.$^{-1}$ band (uncorrected for overla by the 1148 cm.$^{-1}$ band) with solvent refractive index. Solvents, in order of increasing refractive index, are:* 1, 2, 4, 5 *(lower point)*, 6, 7, 9, 10, 13, 14.



(*d*) Excluding the peak solution of benzene in carbon disulphide, the peak density of the 851 cm.$^{-1}$ band increases smoothly with the refractive index of the solvent (Fig. 4). Corresponding data for the 1174 cm.$^{-1}$ band are less complete but the results are broadly similar (Fig. 5). Introduction of a factor involving the molecular volume, as in (*c*), would give a much greater scatter to the points.

(*e*) The peak densities of the 851 and the 1174 cm.$^{-1}$ band maintain an approximately constant ratio for the solvents studied.

(*f*) The behaviour of carbon disulphide solutions differs in several respects from those of the other solvents. The point for carbon disulphide can only with difficulty be accommodated on the band area–solvent property curve (Fig. 3) and as shown in Figs. 4 and 5 the peak densities of the 851 and the 1174 cm.$^{-1}$ band are off the peak density–refractive index curve established by the other solvents. The half-intensity widths of the benzene forbidden bands in benzene are also irregular as in the other solvents a high value of the peak density of the 851 cm.$^{-1}$ band is associated with a low half-intensity width (*e.g.*, in bromoform, sulphur monochloride, and methylene iodide) while in carbon disulphide solution the 851 cm.$^{-1}$ band is one of the broadest. In the case of the allowed bands examined (those at 1970, 1818, and 1033 cm.$^{-1}$) the bands in carbon disulphide solution were narrower than for most other solvents.

(*g*) Quantitative examination of the other forbidden bands was not attempted. A group of three partly resolved bands on the low-frequency side of the strong 1033 cm.$^{-1}$ band is present

in the spectrum of liquid benzene and of solutions, but not in the spectrum of the vapour. As before, these must be ascribed to forbidden fundamental modes. The spectra strongly suggest that they show solvent effects similar to those discussed; in particular, the greater resolution of these three bands in solvents of higher refractive index resulting from decreased band width and increased peak density, is quite striking (Fig. 1). Two weak and barely resolved bands appear at 1312 and 1339 cm.$^{-1}$. There are no binary allowed combination tones that could account for these and, as before, other evidence points to their being forbidden modes. It is reasonable to suppose that they are the B_{2u} (C) mode observed by Mair and Hornig [3] in the spectrum of the solid at 1311 cm.$^{-1}$ and the A_{2g} mode observed by Ingold *et al.*[4] as a forbidden fundamental in the Raman spectrum of the liquid. Alternatively, the 1339 cm.$^{-1}$ band might be the (forbidden) first overtone of the 671 cm.$^{-1}$ fundamental. The 1312 cm.$^{-1}$ band is noticeably intensified in carbon disulphide solution. The other forbidden fundamentals were not examined.

Discussion

Fundamental modes forbidden to be active in absorption have been observed in gases and mixtures of gases at high pressures.[6] Mizushima [7] discussed the case of pressure-induced absorption of symmetric diatomic gases in terms of distortion arising from the field due to the quadrupole moment of the surrounding molecules, and obtained an expression for the integrated absorption intensity in terms of the molecular quadrupole moment, polarisability, and distance of closest approach R_0. In this expression the polarisability and anisotropy of polarisability occur as squared terms and R_0 occurs as an inverse fifth power. Later, Bird [8] discussed the pressure-induced absorption in hydrogen, deuterium, and hydrogen–helium mixtures in terms of an atomic distortion effect produced by overlap of the atoms of the perturbing molecule considered separately, and the quadrupole distortion effect. As in the present work the bands were observed in the liquid state, a fresh factor should be taken into account. The forbidden bands occur because the symmetry of the vibrating molecule is lower in the liquid state, which results in a finite value of the oscillating dipole moment associated with the vibrational transition. However, because the molecule is immersed in a dielectric medium effects connected with electrical displacements in a dielectric then intervene, to enhance the absorption intensity resulting from the original oscillating moment. The magnitude of this enhancement has been discussed by Chako.[9] There is some doubt about the exact correction to be applied, but it appears to be small compared with the observed changes of the integrated intensity of the 851 cm.$^{-1}$ band. Furthermore, only small changes of the integrated intensity, of less than 10%, were found for the 1033 cm.$^{-1}$ allowed band, for the same solvents.

In benzene, finite absorption may arise from causes similar to those discussed by Mizushima and Bird, that is electrical distortion, or through distortion of the geometrical form of the normal mode under the influence of molecular collisions. The latter type of distortion may be described by saying that the inactive fundamental becomes mixed with an active vibrational mode. Thus admixture of either of the infrared active vibrational modes E_u^- or A_{2u} with the inactive modes E_g^+ and B_{2u} will confer activity on these, the A_{2u} out-of-plane hydrogen bending mode at 671 cm.$^{-1}$ being particularly effective as it gives rise to the strongest infrared absorption band in the benzene spectrum.

The importance of the electronic polarisability of the solvent in determining the intensity of the forbidden bands (Fig. 3) suggests that the major part of the intensity comes from distortion of the electron distribution rather than from change in the form of the vibrational mode. The high intensity of the 1174 cm.$^{-1}$ band in carbon disulphide solution discussed below almost certainly excludes the possibility that the intensity of this band arises mainly from distortion of the vibrational mode through admixture of E_u^-

[6] Chisholm and Welsh, *Canad. J. Phys.*, 1954, **32**, 291.
[7] Mizushima, *Phys. Rev.*, 1949, **76**, 1268; 1950, **77**, 150.
[8] Bird, *Physica*, 1951, **17**, 953.
[9] Chako, *J. Chem. Phys.*, 1934, **2**, 644.

character. The dependence of the band area on the solvent function $(n^2 - 1)/(n^2 + 2)V$ (or some similar function) might arise from a dependence on the product of the molar polarisation of the solvent $(n^2 - 1)V/(n^2 + 2)$ and $1/r^6$, where r, the molecular radius of the solvent molecules, is proportional to $V^{1/3}$, making the dependence of integrated intensity similar to that found by Mizushima [7] for the less complicated case of highly compressed symmetrical diatomic gases.

The integrated intensities of the forbidden bands are surprisingly large. Some approximate values are given below for the integrated absorption intensity A, defined by:

$$A = (2{\cdot}303/cl)\int \log_{10}(I_0/I)\,\mathrm{d}\nu$$

where c is the concentration in moles/l., l the path length in cm., and ν in cm.$^{-1}$. $\pi/2$ times the product of peak density and half-intensity width has been used [10] as an approximation for $\int \log_{10}(I_0/I)\,\mathrm{d}\nu$.

Integrated absorption intensities for the 851 *cm.*$^{-1}$ *band.*

Solvent	Carbon disulphide	Methylene bromide	*n*-Tetradecane
$10^{-2}A$	5·3 cm.$^{-1}$	2·0 cm.$^{-1}$	1·3 cm.$^{-1}$

The 1174—1148 cm.$^{-1}$ pair is most intense in carbon disulphide so that overlap from neighbouring bands is least troublesome in this solvent. Decomposition of the 1174—1148 cm.$^{-1}$ pair was effected on the basis of Lorentz-type band shapes [10] of equal half-intensity widths, and approximate integrated absorption intensities calculated as before for the 1174 cm.$^{-1}$ band. The integrated absorption intensity was also calculated for the 1033 cm.$^{-1}$ band for carbon disulphide solution, a small correction being made for the effect of finite slit width. Values of $10^{-2}A$ are: 1174 cm.$^{-1}$ band, 6·1 cm.$^{-1}$; 1033 cm.$^{-1}$ band, 15 cm.$^{-1}$. Because the forbidden 1174 cm.$^{-1}$ band is about three times as wide as the allowed 1033 cm.$^{-1}$ band, the absorption coefficients [defined as $(2{\cdot}303/cl)\log(I_0/I)$] of these two bands become about equal at frequencies 20—30 cm.$^{-1}$ from their respective band maxima. (On the high-frequency side of these bands, the experimental measurements on which these comparisons are based need only small corrections for overlapping of neighbouring bands; on the low-frequency side the comparison rests much more strongly on the reliability of the band shapes found to fit these bands.)

Little is known about the origin and variation of band widths in solution. The widths and shapes of liquid and solution bands probably depend on two main factors: first, the superposition of molecular librational energy changes on the main vibrational energy change, similar to the superposition of rotational energy changes on the main vibrational energy change which is responsible for vapour-phase band contours; and, secondly, perturbations of the energies of the vibrational levels caused by intermolecular forces. For one polyatomic molecule evidence for rotational changes in the liquid similar to those in the vapour has been obtained. Crawford *et al.*[11] examined the Raman spectrum of liquid methane and found wide bands without fine structure, the contours of which could be fitted to the vapour-phase band structures calculated for the same temperature if individual rotational lines were given widths of approximately 55 cm.$^{-1}$. (Individual rotational lines are 21·5 cm.$^{-1}$ apart in the wings of these bands so that at least a greater width than this was necessary to account for absence of rotational structure.) Crawford *et al.* also found greater relative intensity in the Q branch, suggesting that there was a higher proportion of vibrational changes without concomitant rotational changes in the liquid than in the vapour. However, for most substances liquid-phase bands are considerably narrower than the corresponding vapour-phase bands, and a wide variety of molecules, showing diverse rotational band contours, has been found to give bands approximating to a Lorentz band shape in solution or in the liquid phase. These facts suggest that

[10] Cf. Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72.
[11] Crawford, Welsh, and Harold, *Canad. J. Phys.*, 1952, **30**, 81.

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rotation in solution or in the liquid is inhibited or replaced by librational motions and that the energetic contributions from the librational motions are random. This is a reasonable supposition for a molecule such as benzene which has moments of inertia more than twenty times larger than that of methane, with correspondingly greater periods of rotation, and for which the intermolecular forces, judged by heats of vaporisation, are 3—4 times larger than for methane. However it is also possible to account for the band widths by perturbations of the energies of the vibrational levels involved. This may be the major cause of the band width of the 1033 cm.$^{-1}$ band in benzene, which has, for a variety of solutions, an average half-band width of about 10 cm.$^{-1}$. This band is approximately half as wide again as the 1485 cm.$^{-1}$ band belonging to the same symmetry class. By analogy with rotation-vibration bands the effect on the vibrational band shape and width of superposed librational energy changes might be expected to depend mainly on the symmetry of the levels involved and only to a small extent on the other details of the vibrational modes, whereas if the disturbance of the vibrational levels by intermolecular forces is the major cause of the band width the effect would be expected to be bigger for the 1033 cm.$^{-1}$ band, the frequency of which is determined by the forces controlling the motion of the hydrogen atoms on the periphery of the ring, than for the 1485 cm.$^{-1}$ vibration the frequency of which is mainly determined by the forces controlling the motion of the more shielded carbon atoms.

Accordingly it will be assumed that in solution each vibrational mode differs slightly in its energy from molecule to molecule, that is, the molecules show a distribution of values depending on the perturbation momentarily affecting each molecule. For allowed bands the transition moment is probably very nearly constant for all but a very small fraction of the molecules contributing to the absorption band, as generally the frequency width of the band is small compared with its frequency. On these assumptions the band contour of allowed bands represents also the distribution of energy separations of the upper and lower vibrational states of the molecules. For forbidden bands it is clearly not permissible to assume that the transition moment is constant over the frequency range of the band, and the band area has a different meaning from that for allowed bands. These ideas can be applied to compare the half widths and intensities of the 1174 and the 1033 cm.$^{-1}$ band of benzene in CS_2 solution as follows. It seems reasonable to assume, from the similarity of the normal co-ordinates [5] that the distribution of the perturbations of the energy levels of these vibrations in solution will be approximately the same: that is, for both the 1174 and the 1033 cm.$^{-1}$ band approximately the same fraction of molecules will have their ground and their first excited vibrational level so perturbed that they give rise to a vibrational transition x cm.$^{-1}$ from their respective band maxima. If this is so, it follows from the near equality of absorption coefficients when x equals 20—30 cm.$^{-1}$ that the perturbed E_g^+ vibration has there a transmission moment nearly equal to the uniform value of the transition moment for the 1033 cm.$^{-1}$ vibration. On this interpretation, the greater width of the forbidden band springs, not from a greater perturbation of the vibrational states in solution, but from a transition moment that increases outward from the band maximum. Also the value of the variable transition moment for transitions giving rise to the major part of the intensity of this band is comparable with that for the allowed E_u^- band. In view of the relatively small changes of frequency involved (20—30 cm.$^{-1}$ from the band maximum) compared with the frequency separation (140 cm.$^{-1}$) of the 1033 and 1174 cm.$^{-1}$ bands, the major part of the intensity of the 1174 cm.$^{-1}$ band cannot be ascribed to admixture of E_u^- hydrogen bending character.

The plot of peak densities of the 851 and 1174 cm.$^{-1}$ bands against refractive index of the solvent is shown in Figs. 4 and 5. For the 851 cm.$^{-1}$ band the steep increase of peak density with refractive index is due to both the increase in band area and a decrease in half-intensity width with increasing refractive index. The peak densities of the 1033 cm.$^{-1}$ band increase rather similarly with increase in refractive index, but the value for carbon disulphide was in line with the other solvents. The steep increase of peak density

was not continued for solvents of higher refractive index, *viz.*, bromoform and methylene iodide. The cause of this was at least partly that the band half-intensity widths for these solvents are too small compared with the spectral slit widths that could be used. For the 1033 cm.$^{-1}$ band the increase in peak density arose almost entirely from a corresponding decrease in half-intensity width.

Although the high values of the peak densities and band areas found for solutions of benzene in carbon disulphide suggest that some special interaction might be operative, the vapour-pressure data [12] show that such interaction, if present, must be small. The ultraviolet absorption spectrum of 10 μ layers of 1 : 4 and 4 : 1 solutions of benzene in carbon disulphide have been measured and no new bands such as might be expected if charge-transfer interaction were taking place were found at 2600—4000 Å. The authors are indebted to one of the Referees for indicating the need to consider the effect of librational motion on band widths.

THE QUEEN'S UNIVERSITY, BELFAST. [*Received, November 19th*, 1956.]

[12] Hildebrand and Scott, "The Solubility of Nonelectrolytes," Reinhold Publ. Corp., New York, 1950, p. 215.

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315. *The Reaction of Chlorobenzene with Methyl Radicals.*

By A. L. J. BECKWITH and WILLIAM A. WATERS.

Chlorobenzene reacts with free methyl radicals, generated by thermal decomposition of di-*tert.*-butyl peroxide, to give a complex mixture from which a small quantity of 3 : 3′-dichloro-4 : 4′-dimethyldiphenyl has been isolated. The presence of chlorotoluenes has been detected by vapour-phase chromatography, and confirmed chemically in the case of the *para*-isomer.

3 : 3′-Dichloro-4 : 4′-dimethyldiphenyl, 1 : 2-di-(*p*-chlorophenyl)propane, and some related compounds have been synthesised by conventional methods, and 4 : 4′-dichlorodibenzyl has been prepared by dimerisation of 4-chlorobenzyl radicals.

IN a recent investigation [1] of the reactions between anthracene and free methyl radicals, generated by the thermal decomposition of di-*tert.*-butyl peroxide, we found that chlorobenzene was not entirely satisfactory as a solvent since when heated with the peroxide it gave a high-boiling residue, which was separated chromatographically into a yellow amorphous powder and some colourless oils with odours similar to those of the chlorinated diaryls.

From the oily residue of the direct decomposition of di-*tert.*-butyl peroxide in purified chlorobenzene we have now isolated small amounts of a crystalline compound, $C_{14}H_{12}Cl_2$, and this has also been obtained from the reaction of 9 : 10-diphenylanthracene with methyl radicals in chlorobenzene.[2] The infrared spectrum indicated that this product contained 1 : 2 : 4-trisubstituted benzene nuclei and the ultraviolet spectrum was consistent with its formulation as a diphenyl derivative with unsubstituted 2- and 2′-positions. Independent synthesis from 2-chloro-4-iodotoluene shows that it is 3 : 3′-dichloro-4 : 4′-dimethyldiphenyl (III).

The isolation of the substance (III) shows that the attack of free methyl radicals on chlorobenzene occurs, as in methylation of anthracene,[1] by primary *addition* of methyl to give (I), which then dimerises to (II) and is dehydrogenated to (III).

By analogy with the phenylation of chlorobenzene [3] it would be expected that the

[1] Beckwith and Waters, *J.*, 1956, 1108.
[2] Beckwith and Waters, unpublished work.
[3] Augood, Hey, and Williams, *J.*, 1953, 44.

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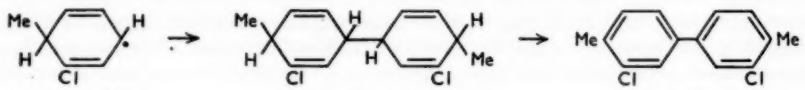
radical (I) would be formed together with *meta*- and *para*-isomers, but just as the early work on the phenylation of compounds C_6H_5R yielded only the least soluble isomer [4] so it appears that the product (III) has been isolated because it is the most symmetrical one of the diphenyl type. Further, addition of methyl radicals to the *meta*- or *para*-position of chlorobenzene would give isomers of radical (I) in which steric hindrance between vicinal



(I) (II) (III)

groups would decrease the probability of dimerisation and subsequent conversion into a di-*ortho*-substituted diaryl. However, various modes of coupling of radical (I) and its isomers may give rise to twenty-one different diphenyl derivatives, and the colourless oils obtained are probably mixtures of such compounds.

In accordance with the mechanism proposed for the methylation of anthracene [1] it would be expected that the radical (I) and its isomers would be converted, by dehydrogenation, into chlorotoluenes. The production of these substances has now been demonstrated by vapour-phase chromatography of the volatile product which gave a curve very similar to that obtained by identical treatment of a mixture of chlorobenzene with *o*- and *p*-chlorotoluene. Unfortunately, the column used was not capable of resolving the chlorotoluene mixture into the separate isomers but the presence of the *para*-compound was confirmed by its oxidation to *p*-chlorobenzoic acid. Several attempts to detect the presence of chloroxylenes were unsuccessful and it appears that, as in the methylation of anthracene, radicals of type (I) do not undergo coupling with a second methyl radical.

The isolation of the above-mentioned products further confirms the general theory that homolytic aromatic substitution occurs by an addition mechanism and that there is no great distinction between the free-radical reactions of alkyl and aryl radicals.

In the Experimental section we also record the syntheses of 1 : 2-di-(*p*-chlorophenyl)-propane and some related compounds by standard methods, and the preparation of 4 : 4′-dichlorodibenzyl by dimerisation of the free *p*-chlorobenzyl radicals produced when di-*tert*.-butyl peroxide is decomposed in *p*-chlorotoluene. These substances were required for comparison with free-radical reaction products.

Experimental

Reaction of Chlorobenzene with Di-tert.-*butyl Peroxide.*—The experiment was conducted as before [1] with 13 g. of the peroxide in purified chlorobenzene (100 ml.). Acetone and *tert*.-butyl alcohol were removed through a fractionating column, and the solvent and remaining volatile products were collected by rapid distillation under reduced pressure. The involatile residue (4·5 g.) was extracted with hot light petroleum (b. p. 40—60°), and the extract was chromatographed on alumina. Elution of the column with 6 : 1 light petroleum–benzene yielded an oil which crystallised from methanol in plates (0·09 g.), m. p. 92°, of 3 : 3′-dichloro-4 : 4′-dimethyldiphenyl (see below). Other fractions were colourless oils (total 1·1 g.) which on oxidation with chromic acid were converted into solid amorphous acids. There was also isolated a yellow gum (2·1 g.) which was precipitated as a powder by the addition of methanol to an ethereal solution.

A sample (20 μl.) of the crude distillate from the free-radical reaction was subjected to vapour-phase chromatography on a column (150 cm. × 6 mm.) packed with a mixture of dinonyl phthalate (45 parts) and graded Celite 545 (100 parts). The column was operated at 130° under reduced pressure with a carrying stream of nitrogen (20 ml./min.), and the fractions were detected by means of a conductivity gauge and recorded graphically. The resultant graph showed an intense peak with a retention time of 25 min. and a very weak band at 47 min. Pure chlorobenzene, similarly treated, showed a single peak at 25 min., while a mixture of equal

[4] Hey, *J.*, 1934, 1966.

parts of chlorobenzene, *o*-chlorotoluene, and *p*-chlorotoluene gave a peak at 25 min. and a band at 47 min. The areas beneath the curves were approximately proportional to the amounts of materials present.

Chlorobenzene was removed from the crude distillate by slow distillation through a short fractionating column, and a sample (10 μl.) of the residue (3·2 g.) was then chromatographed. Peaks were recorded at 25 and 47 min. and the graph was very similar in general shape to that shown by the mixture of chlorobenzene with chlorotoluenes. It was estimated that the residue contained approximately 2 g. of chlorobenzene and 1 g. of chlorotoluenes.

When a sample (0·24 g.) of the residue was oxidised with hot 5% aqueous potassium permanganate the product was a mixture of solid acids (70 mg.), which after 3 crystallisations from water yielded *p*-chlorobenzoic acid (12 mg.), m. p. and mixed m. p. 237°.

Preparation of Reference Compounds.—*2-Chloro-4-iodotoluene.* 3-Chloro-4-methylaniline [5] (15 g.) in 50% (v/v) hydrochloric acid (150 ml.) was diazotised with sodium nitrite solution and treated under cooling with potassium iodide (30 g.) in water (60 ml.). After being heated on the steam-bath for 1 hr. the mixture was extracted with ether, and the product was isolated by distillation under reduced pressure. The iodo-compound, b. p. 123—124°/20 mm., gave crystals, m. p. 22° (lit.,[6] m. p. 8°) (Found: C, 33·6; H, 2·0; total hal., 64·7. Calc. for C_7H_6ClI: C, 33·3; H, 2·4; total hal., 64·3%).

3 : 3′-Dichloro-4 : 4′-dimethyldiphenyl. 2-Chloro-4-iodotoluene (7·1 g.) and copper bronze (8 g.; freshly dried) were heated under nitrogen in a metal-bath at 220°. After 1 hr. the cooled mixture was extracted with hot benzene, and the extract was then passed through a short column of alumina. After removal of the solvent the residual *3 : 3′-dichloro-4 : 4′-dimethyldiphenyl* crystallised from methanol in plates (3·2 g., 90%), m. p. 92° (Found: C, 66·9; H, 4·9; Cl, 28·4. $C_{14}H_{12}Cl_2$ requires C, 66·95; H, 4·8; Cl, 28·2%). The compound showed maximum light absorption (ε 19,000) at 2560 Å, characteristic of diaryls with vacant *ortho*-positions [7] and the infrared spectrum had peaks at 11·4 and 12·4 μ indicating the presence of 1 : 2 : 4-trisubstituted benzene nuclei.

1 : 2-Di-(p-chlorophenyl)propan-2-ol. *p*-Chloroacetophenone (11 g.) in ether (30 ml.) was added dropwise to the Grignard reagent from 4-chlorobenzyl chloride (11·4 g.) in ether (100 ml.), and the mixture was stirred for 1 hr. and then treated with ammonium chloride solution. *1 : 2-Di-(p-chlorophenyl)propan-2-ol* (16·5 g., 83%), which was obtained by removal of the solvent from the ethereal solution, crystallised from light petroleum in needles, m. p. 75° (Found: C, 64·2; H, 5·1. $C_{15}H_{14}OCl_2$ requires C, 64·05; H, 5·0%). Attempts to convert this alcohol into the related chloride were unsuccessful. When the crude mixture obtained by passing dry hydrogen chloride into an ethereal solution was treated with zinc dust in hot acetic acid there were produced small amounts of 1 : 2-di-(*p*-chlorophenyl)propene (see below) and crystals (from methyl acetate) of a compound, m. p. 230°, which may be *1 : 2 : 3 : 4-tetra-(p-chlorophenyl)-2 : 3-dimethylbutane* (Found: C, 68·1; H, 5·05; Cl, 26·3. $C_{30}H_{26}Cl_4$ requires C, 68·2; H, 5·0; Cl, 26·8%).

1 : 2-Di-(p-chlorophenyl)propene. Sulphuric acid (1 ml.) was added to the above-mentioned alcohol (5·0 g.) in acetic acid (20 ml.) and the mixture was heated to boiling. *1 : 2-Di-(p-chlorophenyl)propene* (4·4 g.), which was precipitated by the addition of water to the cooled mixture, crystallised from alcohol in needles, m. p. 110° (Found: C, 68·4; H, 4·5; Cl, 27·0. $C_{15}H_{12}Cl_2$ requires C, 68·45; H, 4·6; Cl, 26·95%). Light absorption in EtOH: max. at 2825 Å (ε 28,400).

1-(p-Chlorophenyl)ethyl chloride. *p*-Chloroacetophenone (20 g.) in ether (100 ml.) was reduced with lithium aluminium hydride (1·3 g.) in the usual way. The crude alcohol was not purified but was converted into the chloride by treatment with phosphorus pentachloride (35 g.) in benzene (100 ml.).[8] The required product was a liquid, b. p. 58—60°/0·9 mm. (Found: C, 55·2; H, 4·75; Cl, 40·2. Calc. for $C_8H_8Cl_2$: C, 54·9; H, 4·6; Cl, 40·5%).

1 : 2-Di-(p-chlorophenyl)propane. 1-(*p*-Chlorophenyl)ethyl chloride (5·4 g.) in benzene (50 ml.) was added to the Grignard reagent from *p*-chlorobenzyl chloride (5·0 g.) in ether (50 ml.), and the mixture was refluxed under nitrogen for 16 hr. The mixture was then treated with dilute hydrochloric acid and, after removal of the solvent, the crude product was chromatographed on alumina. *1 : 2-Di-(p-chlorophenyl)propane* (3·8 g., 60%), which was

[5] Schofield, *J.*, 1927, 2903.
[6] Long and Dains, *Univ. Kansas Sci. Bull.*, 1930, **19**, 205.
[7] O'Shaughnessy and Rodebush, *J. Amer. Chem. Soc.*, 1940, **62**, 2906.
[8] Woodcock, *J.*, 1949, 203.

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eluted with light petroleum, crystallised from methanol in rhombs, m. p. 69° (Found: C, 67·95; H, 5·3; Cl, 26·3. $C_{15}H_{14}Cl_2$ requires C, 67·95; H, 5·2; Cl, 26·75%).

4 : 4′-*Dichlorodibenzyl*. *p*-Chlorotoluene (82 g.) and di-*tert*.-butyl peroxide were refluxed under nitrogen for 22 hr. *tert*.-Butyl alcohol (10·5 g.) was separated by distillation through a fractionating column and unchanged chlorotoluene (66 g.) was removed by steam-distillation. When the residue (12 g.) was distilled under reduced pressure there was obtained 4 : 4′-dichlorodibenzyl (4·1 g.), b. p. 120°/0·2 mm., which crystallised from light petroleum in rhombs, m. p. 102° (Found: C, 67·2; H, 5·0. Calc. for $C_{14}H_{12}Cl_2$: C, 66·95; H, 4·8%).

We are indebted to Messrs. F. Hastings and A. E. Thompson for carrying out the vapour-phase chromatography. One of us (A. L. J. B.) thanks the Commonwealth Scientific and Industrial Research Organisation of Australia for an overseas studentship.

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, November 29th*, 1956.]

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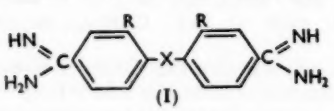
316. *The Search for Chemotherapeutic Amidines. Part XIII.* αω-Di-*p*-amidinophenoxy-alkenes and -alkynes.*

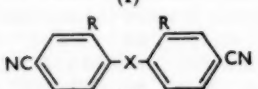
By J. N. ASHLEY and R. D. MACDONALD.

Some αω-di-*p*-amidinophenoxy-alkenes and -alkynes and their nuclear-substituted derivatives have been prepared for comparison with the saturated analogues. They are of no interest as trypanocides.

ALTHOUGH some αω-di-*p*-amidinophenoxyalkanes [1] and their nuclear-substituted derivatives [2] were prepared some years ago, no unsaturated representatives of this class have been described. In continuation therefore of a systematic investigation into the effect on trypanocidal activity of varying the link X in aromatic diamidines of type (I) we have now synthesised a series of diamidines of type (I*a*—*i*). These are considerably less active against *Trypanosoma rhodesiense* than are the saturated analogues. Most are inactive against *T. congolense*; only 1 : 4-di-*p*-amidinophenoxybut-2-yne (I*a*) had a curative action with a chemotherapeutic ratio (LD_{50}/CD_{50}) in mice of approx. 2. The antibacterial activity *in vitro* of some of the compounds was of the same order as that of "Dibromopropamidine" (I; X = O·[CH$_2$]$_3$·O, R = Br).



(I)



(II)

(*a*) X = O·CH$_2$·C≡C·CH$_2$·O; R = H
(*b*) X = O·CH$_2$·C≡C·CH$_2$·O; R = Me
(*c*) X = O·CH$_2$·C≡C·CH$_2$·O; R = Cl
(*d*) X = O·CH$_2$·C≡C·CH$_2$·O; R = Br
(*e*) X = O·CH$_2$·C≡C·C≡C·CH$_2$·O; R = H
(*f*) X = *trans*-O·CH$_2$·CH=CH·CH$_2$·O; R = H
(*g*) X = *cis*-O·CH$_2$·CH=CH·CH$_2$·O; R = H
(*h*) X = *trans*-O·CH$_2$·CH=CH·CH$_2$·O; R = Cl
(*i*) X = *cis*-O·CH$_2$·CH=CH·CH$_2$·O; R = Cl

In most cases the diamidines were prepared by the method of Ashley *et al.*[1] which involved the conversion of the dinitriles (II) into the di-imidoates and thence into the diamidines. The latter were isolated as dihydrochlorides or as the more soluble dimethanesulphonates or di-isethionates. The two diamidines in the *cis*-but-2-ene series were prepared by catalytic hydrogenation of the corresponding but-2-yne compounds.

The αω-di-*p*-cyanophenoxy-alkenes and -alkynes were prepared by condensation of the αω-dichloro- or -dibromo-alkene or -alkyne with the sodium or potassium salt of the appropriate cyanophenol. 2-Chloro- and 2-bromo-4-cyanophenol were prepared by

* Part XII, *J.*, 1956, 368.

[1] Ashley, Barber, Ewins, Newbery, and Self, *J.*, 1942, 103.
[2] Berg and Newbery, *J.*, 1949, 642.

chlorination and bromination, respectively, of *p*-cyanophenol in chloroform.[2] 4-Cyano-2-methylphenol was first described by Paschen [3] who prepared it from 4-formyl-2-methylphenol by converting the formyl group into the oxime and thence by dehydration with acetic anydride into the nitrile. A better preparative method used in the present work involved the conversion of 4-bromo-2-methylphenyl acetate (obtained by successive bromination and acetylation of *o*-cresol) into the 4-cyano-compound by treatment with cuprous cyanide in pyridine with subsequent hydrolysis of the acetoxy-group.

The appropriate dihalogeno-alkenes and -alkynes were prepared by known methods.

Experimental

*4-Bromo-2-methylphenyl Acetate.**—Concentrated sulphuric acid (2·9 c.c.) was added, in one portion, with stirring to 4-bromo-2-methylphenol [4] (498 g.) dissolved in acetic anhydride (325 c.c.). The temperature rose to 75—80° and the solution was then refluxed for 2 hr. After the solution was cooled to 20°, ether (800 c.c.) was added, and the solution was washed successively with water, 2N-sodium carbonate, and water. The *4-bromo-2-methylphenyl acetate* was obtained as a colourless oil (562 g., 93·5%), b. p. 132°/12 mm. (Found: C, 47·4; H, 4·1; Br, 34·6. $C_9H_9O_2Br$ requires C, 47·2; H, 3·9; Br, 34·9%).

4-Cyano-2-methylphenyl Acetate.†—Cuprous cyanide (145 g.) was added, with stirring, during 30 min. to dry pyridine (100 c.c.) at 90°. The reaction was exothermic and the internal temperature rose to 140° (bath-temp., 110—115°). The thick brown mixture was stirred for a further 10 min. and 4-bromo-2-methylphenyl acetate (275 g.) was added. The bath-temperature was raised quickly to 200°; an exothermic reaction occurred and the mixture was then heated (bath-temp. 228—230°) for 3 hr. After being cooled somewhat the reaction mixture was distilled, the bath-temperature being slowly raised to 300° during 45 min. The pale yellow distillate, b. p. 60—170°/20—30 mm., was poured on ice (300 g.), and concentrated hydrochloric acid was added until the mixture was acid to litmus. The white crystalline cyano-compound (177 g., 84%) was filtered off, washed with water, and dried; it had m. p. 75—76°.

4-Cyano-2-methylphenol.†—This was prepared by hot alkaline hydrolysis of the acetate and was obtained (87%) as a white solid, m. p. 93—95°, b. p. 180—182°/12 mm.

Dihalogeno-alkenes and -alkynes.—1 : 4-Dichlorobut-2-yne (70%), b. p. 52—52·5°/10 mm. (Johnson [5] gives b. p. 68—69°/17 mm.), 1 : 4-dibromobut-2-yne [5] (85%), and 1 : 6-dibromohexa-2 : 4-diyne (79%), m. p. 18—19° (Armitage and Whiting [6] give m. p. 16—18°), were prepared by the recorded methods, but the two dibromo-compounds were not distilled. *trans*-1 : 4-Dibromobut-2-ene was prepared essentially as described by Valette.[7] The *cis*-dibromide (54%), b. p. 33·5—34·0°/0·8 mm. (Valette [7] gives b. p. 82°/16 mm.) [from *cis*-1 : 4-dihydroxybut-2-ene [5] (82%), b. p. 128—130°/15 mm.], was heated, with a trace of iodine, at 130—140° for 1 hr.; on cooling, the *trans*-isomer crystallised; it formed colourless plates, m. p. 52—53·5°, from light petroleum (b. p. 40—60°).

αω-Di-p-cyanophenoxy-alkenes and -alkynes.—These *dinitriles* are recorded in Table 1. Three general methods of preparation were used:

(*A*) An alcoholic solution of the cyanophenol (2·2 mol.) followed by 1 : 4-dibromobut-2-yne (1 mol.) was added to a solution of sodium (2·2 atom-equivs.) in dry ethanol (20 c.c. per g. of sodium). The mixture was refluxed overnight and then cooled and filtered. The residue was washed with water and recrystallised from a suitable solvent.

(*B*) 1 : 6-Dibromohexa-2 : 4-diyne (22 g.) was added to a stirred suspension of sodium hydrogen carbonate (17·2 g.) in a solution of *p*-cyanophenol (24·3 g.) in acetone (100 c.c.). The mixture was refluxed, with stirring, overnight, then cooled and filtered. The residue was washed with water and crystallised from acetic acid.

(*C*) 1 : 4-Dichlorobut-2-yne (1 mol.) was added to the cyanophenol (2·2 mol.) dissolved in a solution of potassium hydroxide (2·2 mol.) in alcohol (30 c.c./g.). The mixture was refluxed

* These preparations were carried out by Mr. S. S. Berg.

[3] Pashen, *Ber.*, 1891, **24**, 3671.
[4] Claus and Jackson, *J. prakt. Chem.*, 1888, **38**, 324.
[5] Johnson, *J.*, 1946, 1009.
[6] Armitage and Whiting, *J.*, 1952, 2005.
[7] Valette, *Ann. Chim.* (*France*), 1948, **3**, 644.

overnight and was then cooled and filtered. The residue was washed with water and crystallised from a suitable solvent.

TABLE 1. *Dinitriles.*

Subst.	Method	Yield (%)	M. p.	Found (%) C	H	N	Formula	Required (%) C	H	N
II*a*	*A* [a]	60	159—161°	74·7	4·4	9·65	$C_{18}H_{12}O_2N_2$	75·0	4·2	9·7
II*b*	*A* [a]	40	166—167	76·2	5·2	8·9	$C_{20}H_{16}O_2N_2$	75·9	5·1	8·9
II*c*	*C* [b]	54	224—226	60·9	3·4	7·9	$C_{18}H_{10}O_2N_2Cl_2$ [c]	60·5	2·8	7·8
II*d*	*C* [b]	50	220—222	48·6	2·6	6·4	$C_{18}H_{10}O_2N_2Br_2$ [d]	48·4	2·2	6·3
II*e*	*B* [a]	49	195—197	77·0	4·2	8·8	$C_{20}H_{12}O_2N_2$	76·95	3·85	9·0
II*f*	*A* [a]	70	204—206	75·0	5·05	9·6	$C_{18}H_{14}O_2N_2$ [e]	74·5	4·8	9·65
II*h*	*C* [a]	61	207—209	60·1	3·6	7·7	$C_{18}H_{12}O_2N_2Cl_2$	60·2	3·4	7·8

[a] Cryst. from acetic acid. [b] Cryst. from pyridine. [c] Found: Cl, 19·9. Required: Cl, 19·9%. [d] Found: Br, 35·7. Required: Br, 35·9%. [e] Found: Cl, 19·5. Required: Cl, 19·8%.

TABLE 2. *Diamidines.*

Subst.	Alcohol (and diluent) used in preparation of di-imidoate	Solvent for crystn.	M. p.
I*a*	EtOH [a] ($CHCl_3$)	MeOH–$COMe_2$	245—247°
I*b*	EtOH [a] ($CHCl_3$)	MeOH	308—310 [b]
I*c*	EtOH (dioxan)	MeOH–Et_2O	243—245
I*d*	EtOH	MeOH	253—255
I*e*	EtOH	Dil. HO·$[CH_2]_2$·SO_3H	272—274 [b]
I*f*	EtOH	Dil. Me·SO_3H	274—276
I*g*	—	MeOH	232—234
I*h*	HO·$[CH_2]_2$·OEt	MeOH	236—238
I*i*	—	—	218—220

Subst.	Formula	Found (%) followed by required (%) C	H	N	Halogen or S
I*a*	$C_{18}H_{18}O_2N_4,2HCl,2H_2O$ [c]	50·5	5·5	13·0	16·5 (Cl)
		50·1	5·6	13·0	16·5
I*b*	$C_{20}H_{22}O_2N_4,2MeSO_3H$	48·75	5·8	10·2	11·9 (S)
		48·7	5·5	10·3	11·8
I*c*	$C_{18}H_{16}O_2N_4Cl_2,2HO·[CH_2]_2·SO_3H,0·5H_2O$ [d]	40·15	4·5	8·25	10·85 (Cl)
		40·4	4·4	8·6	10·8
I*d*	$C_{18}H_{16}O_2N_4Br_2,2HO·[CH_2]_2·SO_3H$	36·0	3·6	7·5	21·9 (Br)
		36·1	3·8	7·7	21·85
I*e*	$C_{20}H_{18}O_2N_4,2HO·[CH_2]_2·SO_3H$	48·2	5·2	9·3	10·7 (S)
		48·2	5·0	9·35	10·7
I*f*	$C_{18}H_{20}O_2N_4,2Me·SO_3H$	46·8	5·7	10·8	12·3 (S)
		46·6	5·4	10·85	12·4
I*g*	$C_{18}H_{20}O_3N_4,2Me·SO_3H$	46·3	5·7	10·75	11·9 (S)
		46·6	5·4	10·85	12·4
I*h*	$C_{18}H_{16}O_2N_4Cl_2,2HO·[CH_2]_2·SO_3H$	40·6	5·0	8·4	11·1 (Cl)
		40·8	4·7	8·7	11·0
I*i*	$C_{18}H_{16}O_2N_4Cl_2,2HO·[CH_2]_2·SO_3H$	40·5	4·9	8·6	10·9 (Cl)
		40·8	4·7	8·7	11·0

[a] In these preparations the dinitriles were in solution when the mixture was saturated with HCl. In the other cases the dinitriles were present in suspension. [b] Decomp. [c] Found: H_2O, 8·5. Required: H_2O, 8·35%. [d] Found: H_2O, 1·5. Required: H_2O, 1·4%.

Preparation of Diamidines.—The dinitriles were suspended or dissolved in the appropriate alcohol (often in presence of a diluent), and the mixture was saturated with hydrogen chloride while being kept at 0—10°. The di-imidoate dihydrochlorides were gradually formed and after several days were filtered off, dried in a vacuum at room temperature, and added to saturated alcoholic ammonia (10 c.c./g. of solid) and the mixture was heated at 50—60° for 5—6 hr. The *diamidines* which are recorded in Table 2 were isolated by standard procedures.

cis-1 : 4-*Di*-p-*amidinophenoxybut*-2-*ene* (I*g*).—1 : 4-Di-*p*-amidinophenoxybut-2-yne dihydrochloride in methanol was hydrogenated in presence of 10% w/w palladium–calcium carbonate at room temperature. The uptake of hydrogen was stopped when 1 mol. had been absorbed.

The catalyst was then filtered off, and after removal of the solvent the diamidine dihydrochloride was converted into the dimethanesulphonate (70%) which was crystallised from methanol.

cis-1 : 4-*Di*-(4-*amidino*-2-*chlorophenoxy*)*but*-2-*ene* (I*i*).—This was prepared similarly; after hydrogenation, most of the solvent was evaporated and the gummy dihydrochloride, which was precipitated by addition of acetone, was obtained as a white powder after trituration with acetone.

The authors thank Dr. H. J. Barber, F.R.I.C., for his interest, Mrs. R. Stone, B.Sc., and Mr. W. A. Freeman for the biological tests, Mr. S. Bance, B.Sc., A.R.I.C., for the semimicro-analyses, and the Directors of May & Baker Ltd. for permission to publish these results.

THE RESEARCH LABORATORIES, MAY & BAKER, LTD.,
DAGENHAM, ESSEX. [*Received, November* 30*th*, 1956.]

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317. *Benziminazole Analogues of Biologically Active Indole Derivatives.*

By R. FOSTER, H. R. ING, and E. F. ROGERS.

The benziminazole analogue of 5-hydroxytryptamine, *viz.*, 1-2′-aminoethyl-6-hydroxybenziminazole, has been prepared. 6-Amino-1-ethyl-2-methylbenziminazole and its N^6-methyl derivative have been synthesised as possible antagonists of 5-hydroxytryptamine.

CONSIDERABLE interest has been taken in recent years in the effect on biological activity of replacing an aryl nucleus in an active compound by a different nucleus. Sometimes this replacement does not alter the type of biological activity, or even change the potency greatly; *e.g.*, α-thienylalkylamines resemble the analogous phenylalkylamines closely in hypertensive activity,[1] and 2-thenoic esters of alkamines resemble the corresponding benzoic esters as local anæsthetics (cf. 2-thenoylecgonine methyl ester and cocaine [2]). On the other hand, pyrithiamine is a powerful antagonist of thiamine.[3] We have been interested in the replacement of the indole by the benziminazole nucleus. Mamalis, Petrow, and Sturgeon [4] prepared β-1-benziminazolylalanine but it had a negligible effect upon the growth of a variety of micro-organisms and presumably does not inhibit the utilization of tryptophan. We have prepared the benziminazole analogue (V; R = OH) of 5-hydroxytryptamine (serotonin) in order to discover whether it resembles or differs from serotonin in its pharmacological action.

As a model reaction sequence 1-2′-aminoethylbenziminazole (V; R = H) was first prepared by the series of reactions (I—V). This analogue of tryptamine had already been made by Mamalis *et al.*[4] who used a different route to the diamine (III; R = H), devised by Karrer and Naef.[5] When 3-chloro-4-nitroanisole (I; R = OMe) was used as a starting material, reduction of the nitroamine (II; R = OMe) and cyclisation of the product (III; R = OMe) were achieved in one operation by using formic acid as solvent; this device obviated the difficulty of isolating the very unstable *o*-diamine (III; R = OMe). The compound (IV; R = OMe) gave 1-2′-aminoethyl-6-methoxybenziminazole (V; R = OMe) with hydrazine and 1-2′-aminoethyl-6-hydroxybenziminazole (V; R = OH) with hot hydrobromic acid. Both bases were isolated as dipicrates.

Acetylation of the diamine (III; R = H) gave a diacetyl derivative which was cyclised

[1] Blicke and Burckhalter, *J. Amer. Chem. Soc.*, 1942, **64**, 477.
[2] Steinkopf and Ohse, *Annalen*, 1924, **437**, 14.
[3] Woolley and White, *J. Biol. Chem.*, 1943, **149**, 285.
[4] Mamalis, Petrow, and Sturgeon, *J.*, 1950, 1600.
[5] Karrer and Naef, *Helv. Chim. Acta*, 1936, **19**, 1029.

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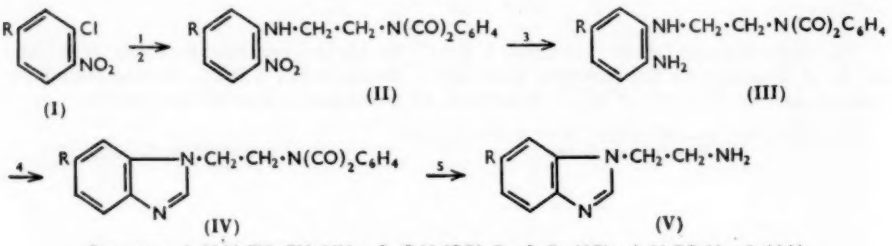
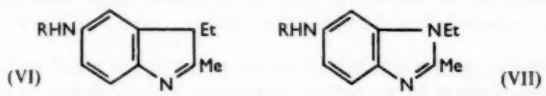
with phosphorus oxychloride; treatment of the product with hydrazine gave 1-2′-aminoethyl-2-methylbenziminazole which was isolated as its dihydrochloride. 1-2′-Aminoethyl-2-phenylbenziminazole (isolated as its dihydrochloride) was obtained directly when the dibenzoyl derivative of the diamine (III; R = H) was treated with hydrazine. A similar cyclisation did not occur with the diacetyl derivative.



Reagents: 1, $H_2N{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2$; 2, $C_6H_4(CO)_2O$; 3, Fe–HCl; 4, $H{\cdot}CO_2H$; 5, N_2H_4

Woolley and Shaw [6] have shown that 5-amino-3-ethyl-2-methylindole (VI; R = H) inhibits the stimulant action of serotonin on isolated segments of sheep carotid artery, and that this inhibitory action is increased 150-fold by methylation of the 5-amino-group, *i.e.*, in (VI; R = Me). We have therefore prepared the benziminazole analogues (VII; R = H and Me) of these two indole derivatives. In making these compounds we relied



upon Philips's observation [7] that methylation of 2-methyl-5(6)-nitrobenziminazole with dimethyl sulphate in the absence of alkali gives mainly 1 : 2-dimethyl-6-nitrobenziminazole, and have assumed that ethylation with diethyl sulphate under the same conditions will also occur mainly at the nitrogen atom *meta* to the nitro-group. Philips proved the structure of his main methylation product by synthesis of 1 : 2-dimethyl-6-nitrobenziminazole from 2-chloro-*N*-methyl-5-nitroaniline, but we were unable to replace the chlorine atom in 2-chloro-*N*-ethyl-5-nitroethylaniline by an amino-group, even under more drastic conditions than Philips used; not could we replace the chlorine atom in 2-chloro-5-nitroaniline by ethylamino.

Ethylation of 2-methyl-5(6)-nitrobenziminazole gave two products in the proportion of 8 : 1 by weight. The more abundant isomer was assumed to be 1-ethyl-2-methyl-6-nitrobenziminazole. Catalytic reduction of the nitro-group gave 6-amino-1-ethyl-2-methylbenziminazole; reduction of the formyl derivative of this base with lithium aluminium hydride gave the 6-methylamino-compound, which was isolated as its dipicrate.

Experimental

1-2′-*Aminoethyl*-6-*hydroxybenziminazole*.—A mixture of 3-chloro-4-nitroanisole [8] (15 g.), ethylenediamine (24 g.), and anhydrous cupric chloride (1·5 g.) was heated to 50° with stirring. After a few minutes the mixture began to boil and heating was discontinued until the vigorous reaction subsided, then the mixture was heated for 1 hr. on the steam-bath. Excess of ethylene diamine was removed *in vacuo* (steam-bath) and N-(*3-methoxy-6-nitrophenyl*)*ethylenediamine hydrochloride* obtained from the residue by crystallisation from 0·5N-hydrochloric acid (yield 76%) (Found: C, 43·3; H, 5·6. $C_9H_{14}O_3N_3Cl$ requires C, 43·6; H, 5·7%). This product (14·5 g.) was heated with phthalic anhydride (21 g.) in pyridine (40 ml.) at 100° for 6 hr. The mixture was diluted with water, and the solid *5-methoxy-2-nitro*-N-*2′-phthalimidoethylaniline* (II;

[6] Woolley and Shaw, *J. Pharmacol.*, 1950, **111**, 43.
[7] Philips, *J.*, 1931, 1143.
[8] Hodgson and Hanley, *J.*, 1926, 543.

R = OMe) recrystallised from dioxan, as yellow needles, m. p. 208° (96%) (Found: C, 59·7; H, 4·4; N, 12·3. $C_{17}H_{15}O_5N_3$ requires C, 59·8; H, 4·4; N, 12·3%). The phthalimido-compound (21 g.) in 98—100% formic acid (70 ml.) and water (250 ml.) was reduced by iron powder (35 g.) and hydrochloric acid (30 ml.), the acid being added dropwise to the hot (steam-bath) stirred mixture during 2 hr. The product, obtained as a gum from the cooled mixture by extraction with chloroform, crystallised from aqueous alcohol. *6-Methoxy-1-2′-phthalimidoethylbenziminazole* (IV; R = OMe) had m. p. 174° (yield 37%) (Found: C, 67·2; H, 4·8; N, 13·2. $C_{18}H_{15}O_3N_3$ requires C, 67·3; H, 4·7; N, 13·1%). The phthaloyl group was removed by hydrazine and *1-2′-aminoethyl-6-methoxybenziminazole dipicrate* isolated as yellow needles, m. p. 214—218° (decomp.) (from aqueous alcohol) (Found: C, 40·7; H, 3·1; N, 19·8. $C_{10}H_{13}ON_3,2C_6H_3O_7N_3$ requires C, 40·7; H, 2·9; N, 19·4%). Both the *O*-methyl and the phthaloyl group were removed by boiling the methoxyphthalimidoethylbenziminazole (6 g.) with 46—48% hydrobromic acid (100 ml.) for 5 hr. The mixture was diluted with water (100 ml.), phthalic acid removed by filtration, and the filtrate evaporated *in vacuo* at 100°. The dark violet residue was dissolved in dilute aqueous ammonia, and the solution left until excess of ammonia had evaporated. Addition of saturated aqueous picric acid precipitated crude *1-2′-aminoethyl-6-hydroxybenziminazole dipicrate* (30%). Four crystallisations from aqueous alcohol (50% v/v) gave red prisms, which decomposed above 140° (Found: C, 39·0; H, 2·8; N, 19·8. $C_9H_{11}ON_3,2C_6H_3O_7N_3$ requires C, 39·7; H, 2·7; N, 19·8%).

1-2′-Aminoethyl-2-methylbenziminazole.—*N*-*o*-Nitrophenylethylenediamine [9] was converted into its phthaloyl derivative which, crystallised from acetone, had m. p. 176° (Karrer and Naef [5] record m. p. 184°). This crude product (25 g.) was reduced by stirring it for 6 hr. with iron powder (25 g.) in refluxing ethanol, 2N-hydrochloric acid being added at the rate of 1 ml. per ½ hr. The hot mixture was filtered and the filtrate diluted with a large volume of water; *N*-2′-phthalimidoethyl-*o*-phenylenediamine (II; R = H) crystallised slowly; it had m. p. 124—125° after two crystallisations from alcohol (Karrer and Naef [5] record m. p. 124°). Acetylation with acetic anhydride gave *NN′-diacetyl-N-2′-phthalimidoethyl-o-phenylenediamine*, m. p. 192—193° after crystallisation from chloroform–acetone (Found: N, 11·6. $C_{20}H_{19}O_4N_3$ requires N, 11·5%). The diacetyl compound (3 g.) was cyclised by boiling phosphorus oxychloride (15 ml.) for 3 hr. The solution was diluted with water and extracted with chloroform.

2-Methyl-1-2′-phthalimidoethylbenziminazole so obtained, and crystallised from acetone–ether, had m. p. 170° (Found: C, 70·4; H, 5·3; N, 13·7. $C_{18}H_{15}O_2N_3$ requires C, 70·8; H, 4·9; N, 13·8%). This phthalimido-compound was treated with an equal weight of hydrazine hydrate in boiling alcohol for 10 hr. The mixture was acidified and filtered and the base extracted with chloroform. The residue after removal of the chloroform was dissolved in dilute hydrochloric acid and the acid solution evaporated *in vacuo*. *1-2′-Aminoethyl-2-methylbenziminazole dihydrochloride* was crystallised twice from methanol–acetone; it did not melt below 250° (Found: N, 16·7. $C_{10}H_{15}N_3Cl_2$ requires N, 17·0%).

1-2′-Aminoethyl-2-phenylbenziminazole.—*N*-2-Phthalimidoethyl-*o*-phenylenediamine (10 g.) was heated with benzoic anhydride (40 g.) for 4 hr. at 100°. *NN′-Dibenzoyl-N-2′-phthalimidoethyl-o-phenylenediamine*, recrystallised from chloroform–acetone, had m. p. 197—198° (Found: N, 8·5. $C_{30}H_{23}O_4N_3$ requires N, 8·8%). Hydrazinolysis of this product as described above for the 2-methylbenziminazole compound gave *1-2′-aminoethyl-2-phenylbenziminazole dihydrochloride*; recrystallised from methanol–acetone, it did not melt below 250° (Found: N, 13·8. $C_{15}H_{17}N_3Cl_2$ requires N, 13·6%).

6-Amino-1-ethyl-2-methyl- and 1-Ethyl-2-methyl-6-methylamino-benziminoazole.—2-Methyl-5(6)-nitrobenziminazole (10 g.), obtained by nitration [10] of 2-methylbenziminazole,[11] was heated with diethyl sulphate (7·5 ml.) at 140° for 7 hr. The mixture was basified with 4N-sodium hydroxide, and the solid collected. Some 40% of unchanged starting material was recovered from the filtrate by acidification with acetic acid and this amount was not decreased by prolonging the reaction time. The ethylated product (yield, 30—40%) was crystallised first from aqueous alcohol or water and then from benzene. The latter solvent revealed the presence of two isomers. The less soluble isomer, m. p. 176°, constituting one-ninth of the total product, was assumed to be *1-ethyl-2-methyl-5-nitrobenziminazole* (Found: C, 58·7; H, 5·5. $C_{10}H_{11}O_2N_3$ requires C, 58·5; H, 5·4%). The more soluble isomer, m. p. 142° after

[9] Linsker and Evans, *J. Org. Chem.*, 1945, **10**, 283.
[10] Fisher and Hess, *Ber.*, 1903, **36**, 3967.
[11] Philips, *J.*, 1928, 2393.

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crystallisation from benzene and finally from water or aqueous alcohol, was assumed to be 1-*ethyl*-2-*methyl*-6-*nitrobenziminazole* on the basis of Philips's methylation of 2-methyl-5(6)-nitrobenziminazole [7] (Found : C, 58·5; H, 5·6%). It was reduced catalytically in alcoholic suspension over Raney nickel at 3 atm. for 3 hr. 6-*Amino*-1-*ethyl*-2-*methylbenziminazole*, crystallised from benzene–light petroleum (b. p. 60—80°), had m. p. 174° (Found : C, 68·4; H, 7·4; N, 24·4. $C_{10}H_{13}N_3$ requires C, 68·6; H, 7·4; N, 24·0%). The *monopicrate* (from water) had m. p. 205° (Found : C, 47·5; H, 4·0; N, 20·7. $C_{10}H_{13}N_3,C_6H_3O_7N_3$ requires C, 47·5; H, 4·0; N, 20·8%). A solution of the free base in 98—100% formic acid was distilled slowly for 6 hr., toluene being added dropwise; water and toluene distilled over through a Dufton column. The mixture was diluted with water, and the aqueous layer separated and evaporated to dryness *in vacuo*. The residue was taken up in water, basified with sodium hydrogen carbonate, and extracted with chloroform. The dried extract (Na_2SO_4) gave on evaporation 1-*ethyl*-6-*formamido*-2-*methylbenziminazole* which, crystallised from ethyl methyl ketone, had m. p. 170° (yield 40%) (Found : C, 64·7; H, 6·5; N, 20·3. $C_{11}H_{13}ON_3$ requires C, 65·0; H, 6·4; N, 20·7%). The formyl compound (0·25 g.) in tetrahydrofuran (20 ml.) was added slowly to a suspension of lithium aluminium hydride (1 g.) in tetrahydrofuran (20 ml.) and the mixture then boiled with stirring for 1½ hr. The product, extracted with ether after decomposition of excess of lithium aluminium hydride, did not crystallise; it was converted into 1-*ethyl*-2-*methyl*-6-*methylaminobenziminazole dipicrate* which crystallised from aqueous alcohol and decomposed above 140° (yield 80%) (Found : C, 42·5; H, 3·2; N, 19·7. $C_{11}H_{15}N_3,2C_6H_3O_7N_3$ requires C, 42·6; H, 3·2; N, 19·5%).

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318. *Amine Compounds of the Transition Metals. Part I. The Reaction of Vanadium Tetrachloride with Some Aliphatic Amines.*

By G. W. A. FOWLES and C. M. PLEASS.

The reaction of vanadium tetrachloride with mono-, di-, and tri-methylamine has been studied over a wide range of experimental conditions; simple 1 : 1 adducts form at low amine concentrations, but with increasing amine : VCl_4 ratios more extensive reaction occurs. Compounds isolated and identified include $VCl_2(NHMe)_2,NH_2Me$, $VCl_2(NMe_2)_2$, and $VCl_3(NMe_3)_2$; their precise nature has been established by measuring their magnetic moments, and their molecular weights in nitrobenzene solution. Probable reaction mechanisms and the structure of the isolated products are discussed.

IONIC halides of metals of Groups IA, IIA, and IIIA form simple addition compounds—ammoniates—with ammonia, in which the ammonia molecules are bound to the metal by relatively weak forces [1] of the order of 8—20 kcal./mole. With the transition-metal ions, however, *e.g.*, Cr^{3+} and Co^{3+}, much stronger bonds may be formed between the metal ion and the ammonia molecules, because the metal ions can form donor–acceptor bonds by accepting electrons (from the nitrogen atoms) into their inner *d* orbitals. Some of the metal ions do however form weaker bonds because they make use of their outer *d* orbitals for the bond formation (*e.g.*, Cr^{2+}, Ni^{2+}).[2] Whereas the ammonia molecules are bonded unchanged in both the ammoniates and the co-ordination compounds, we find a different type of behaviour with the more covalent halides of a number of metals in the main groups around the centre of the Periodic Table (Be, B, Si, Ge, Sn, Pb, As, Sb, and Bi), and with most transition-metal halides in which the metal is in its highest valency state, since the initial co-ordination of the ammonia molecules is followed by the elimination of the

[1] Biltz, *Z. anorg. Chem.*, 1923, **130**, 93.
[2] Cartmell and Fowles, " Valency and Molecular Structure," Butterworths, London, 1956, p. 184.

hydrogen halide and the formation of either ammonobasic halides or amides; the partial replacement of halogen atoms by NH_2 groups gives the ammonobasic halides, and complete replacement the amides.

The reaction of a number of transition-metal chlorides with ammonia has been examined recently by Fowles and Pollard,[3] who showed that as the metal–chlorine bond becomes more ionic, *e.g.*, in $SiCl_4$, $TiCl_4$, $ZrCl_4$, and $ThCl_4$, so the replacement of Cl atoms by NH_2 groups is less complete; such compounds as $Si(NH_2)_4$, $TiCl(NH_2)_3$, $ZrCl_3(NH_2)$, and $ThCl_4,6NH_3$ were reported. With the ammonobasic halides, structural investigations such as molecular-weight determinations are not possible, since the compounds are usually insoluble in all solvents with which they do not react and are probably polymeric. Now amines should yield substances which are more amenable to structural investigation than the ammonobasic chlorides, since there are fewer hydrogen atoms directly bound to the nitrogen atom, so that elimination of hydrogen chloride is less likely, and polymerisation (by subsequent elimination between neighbouring molecules) is reduced.

By analogy with their reaction with ammonia, we would expect the more ionic halides of Groups IA, IIA, and IIIA to form simple addition compounds with amines, and this has been confirmed by the preparation of amine complexes of lithium halides,[4] calcium chloride,[5] and the rare-earth chlorides.[6]

Little reliable work has been published concerning the reaction of amines with the transition-metal halides. Dermer and Fernelius [7] reported the formation of addition compounds of titanic chloride and aromatic amines, and they obtained $Ti(NPh_2)_4$ by the reaction of the chloride with $NaNPh_2$; the compound $Ti(NPh_2)_4$ is rather unexpected on steric grounds, since there seems to be insufficient room around the titanium atom to accommodate the four NPh_2 groups. More recently, Troost [8] reported the formation of a number of addition compounds of this chloride with various aliphatic amines, although he merely analyses the product and gives an overall formula to the adduct without emphasing the possibility that replacement may have occurred. Antler and Laubengayer [9] made a much fuller study of the gaseous phase reactions of titanic chloride with ammonia and mono-, di-, and tri-methylamine, and found that in addition to replacement of chlorine atoms by amino-residues there is also some reduction to Ti(III); this reduction is only significant however in the $TiCl_4$–NMe_3 reaction where $TiCl_3,2NMe_3$ was isolated.

Almost no work has been carried out on the amine compounds of the Group VA elements. Some early investigations of Mertes and Fleck [10] indicated that vanadium tetrachloride reacts with most amines, but the results have little value since they were not carried out under rigorously anhydrous conditions; indeed, a number of analytical figures are accounted for by assuming water molecules to be present in the complexes. A similar criticism must be made of the cursory study of the VCl_4–NH_3 reaction due to van Valkenburg and Schoffman.[11]

Because of this unsatisfactory situation, we are carrying out a systematic investigation of the reaction of amines with the transition-metal halides, and in this paper we report an investigation of the reaction of vanadium tetrachloride with mono-, di-, and tri-methylamine. Any simple 1 : 1 addition compounds would constitute complexes of the unusual co-ordination number five.

Experimental

Materials.—Vanadium tetrachloride was prepared by the action of chlorine on vanadium-metal powder (99% pure) at 400° in an all-glass apparatus; traces of oxide in the metal were

[3] Fowles and Pollard, *J.*, 1953, 4128.
[4] Simon and Glauner, *Z. anorg. Chem.*, 1929, **178**, 177.
[5] Maillard, *Compt. rend.*, 1936, **203**, 187.
[6] Popov and Wendtlandt, *J. Amer. Chem. Soc.*, 1955, **77**, 857.
[7] Dermer and Fernelius, *Z. anorg. Chem.*, 1953, **221**, 83.
[8] Troost, *Canad. J. Chem.*, 1952, **30**, 835, 842.
[9] Antler and Laubengayer, *J. Amer. Chem. Soc.*, 1955, **77**, 5250.
[10] Mertes and Fleck, *Ind. Eng. Chem.*, 1915, **7**, 1037.
[11] van Valkenburg and Schoffman, Univ. Colorado Studies, Ser. D1, No. 1, 1940, p. 23.

removed by reduction with hydrogen before chlorination. The vanadium tetrachloride was collected in an ice-cooled container and sealed off *in situ*; it was degassed by pumping out dissolved chlorine through the stopcock (greased with Silicone grease) attached to the container, and finally distilled into ampoules which were sealed off. The purity of the tetrachloride was confirmed by analysis (Found : V, 26·8; Cl, 73·9. Calc. for VCl_4 : V, 26·4; Cl, 73·6%).

Vanadium trichloride was made by the thermal decomposition of vanadium tetrachloride in an atmosphere of carbon dioxide.[12]

Trimethylamine (from Messrs. British Drug Houses) was dried and freed from traces of primary and secondary amines by distillation *in vacuo* from phosphoric oxide.[13]

Dimethylamine (from Messrs. British Drug Houses) was dried by repeated distillation *in vacuo* from freshly crushed barium oxide, followed by a final treatment with freshly distilled titanium tetrachloride. Titanium tetrachloride was used for the final drying, since both it and the products it forms with dimethylamine are very sensitive to traces of moisture.

Monomethylamine was obtained in an anhydrous state from a 30 w/w aqueous solution (from Messrs. British Drug Houses) by distillation *in vacuo* on to freshly crushed barium oxide; only the first 20—25% was collected, and this was treated in a similar manner a further 3—4 times, and finally allowed to react with titanium tetrachloride or a thin film of potassium metal.

Chlorobenzene and " iso-octane " (2 : 2 : 4-trimethylpentane) were each fractionated in an efficient Fenske column, only the middle fractions being taken, and finally distilled from phosphoric oxide.

Nitrobenzene (from Messrs. May and Baker) was fractionally crystallised four times and distilled (still surface) *in vacuo* from phosphoric oxide directly into the molecular-weight apparatus.

Analyses.—Wherever possible, the products were completely analysed, but on occasion the product firmly adhered to the vessel walls and could not be removed; it was then hydrolysed *in situ*, so that the subsequent analysis gave only the V : Cl : N ratio.

Nitrogen was determined by distilling the amine from an alkaline solution into an excess of standard sulphuric acid and back-titration with standard sodium hydroxide solution (B.D.H. 4·5 indicator). Any amine present was always removed in this way before the estimation of vanadium, since it interfered with the vanadium(IV)–potassium permanganate titration.

Vanadium was determined in dilute sulphuric solution by reduction with sulphur dioxide, removal of excess of sulphur dioxide with nitrogen, and titration with standard potassium permanganate solution at 70°.[14]

Chlorine was determined by the Volhard method, with an occasional gravimetric silver chloride check.

Reactions.—Reactions were studied under rigorously anhydrous conditions in vacuum systems.

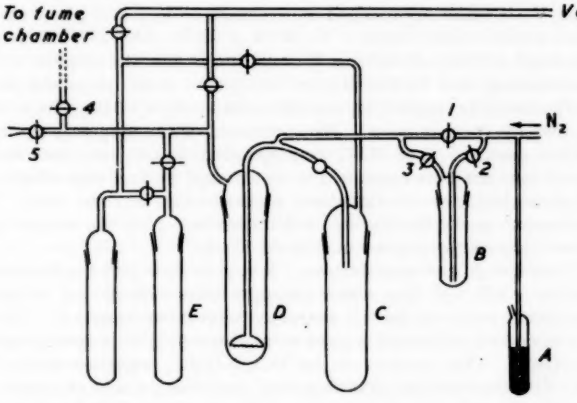
(a) *Vanadium chloride and dimethylamine.* This reaction is described first in the greatest detail since it was investigated the most fully; the products are potentially the simplest, since there is only one replaceable hydrogen atom in the amine.

(1) Preparation by passing dimethylamine vapour (in a stream of nitrogen) into a solution of the chloride in " iso-octane." The solution of chloride in " iso-octane " was prepared in reaction vessel *D* (Figure) by breaking an ampoule of chloride *in vacuo* and condensing it into *D via* tap 5, then condensing it in dried " iso-octane " from reservoir E. The contents of vessel *D* were allowed to warm to room temperature and then agitated with a stream of oxygen-free nitrogen (dried by passage through vertical 70 cm. columns of magnesium perchlorate and phosphoric oxide). As soon as the pressure in the reaction vessel became equal to the head of of mercury in bubbler *A*, tap 4 was opened and the nitrogen allowed to pass to the fume chamber through a drying tube of silica gel. By closing tap 1 and opening taps 2 and 3, the nitrogen stream was passed through the trap *B* of liquid dimethylamine held at −78° until dimethylamine could be freely detected in the gases issuing from the fume chamber outlet; the reaction was then assumed to be complete. The solvent was then drawn through the sinter-pad into vessel *C*; fresh solvent was distilled into *D*, the suspension agitated with nitrogen, and the solvent again drawn off into *C*; this procedure was repeated until no trace of colour remained in the solvent, so that all traces of unchanged tetrachloride were removed. The buff-coloured *product* remaining in *D* was evacuated for 3—4 hours and then shaken into a weighed vessel

[12] *Inorg. Synth.*, **4**, 128.
[13] Brown, Taylor, and Gerstein, *J. Amer. Chem. Soc.*, 1944, **66**, 431.
[14] Hillebrand, Lunden, Bright, and Hoffman, " Applied Inorganic Analysis," 2nd Edn., Wiley, New York, 1953, p. 458.

for analysis [Found: (i) V, 20·9; Cl, 57·1; N, 7·0%; V : Cl : N ratio, 1 : 3·92 : 1·19. (ii) V, 21·4; Cl, 57·3; N, 6·9%; ratio 1 : 3·96 : 1·15. VCl_4,$NHMe_2$ requires V, 21·4; Cl. 59·5; N, 5·9%].

When this product was heated *in vacuo* to 150° for 1—2 hr.—conditions under which dimethylammonium chloride readily sublimes—a very small amount of this chloride (coloured slightly by a trace of vanadium-containing material) sublimed away, leaving the bulk of the product almost unchanged (Found: V, 21·0; Cl, 57·4; N, 7·2%).



When the amine concentration in the initial reaction was increased by raising the bath temperature to −35°, and lowering that of the vanadium tetrachloride–" iso-octane " solution to −23°, the nature of the *product* changed noticeably, and the buff product was heterogeneous and mixed with a red substance (Found: V, 15·2; Cl, 42·6; N, 12·5%; V : Cl : N, 1 : 4·05 : 2·99. VCl_3·NMe_2,$NHMe_2$ + NH_2Me_2Cl requires V, 15·5; Cl, 43·2; N, 12·8%).

Note. The apparatus shown in the Figure includes the additional taps, etc., that are necessary for the washing and recycling of solvents in subsequent reactions.

The product prepared with the higher concentration of amine vapour was agitated with liquid dimethylamine at −78° for 1 hr. by means of a stream of nitrogen; the initial product then largely dissolved to give a deep red solution. The amine was distilled from the product, the solid remaining being pumped at room temperature for 2 hr. The heterogeneous product, which contained a considerably greater proportion of red constituent than it did before, was hydrolysed *in situ* and gave an analysis corresponding to a V : Cl : N ratio of 1 : 3·94 : 3·78, *i.e.*, $VCl_3(NMe_2)_2$ + $2NH_2Me_2Cl$. When this product was washed with chlorobenzene, the extract gave a solid (on removal of chlorobenzene) which was hydrolysed *in situ* and gave an analysis corresponding to V : Cl : N = 1 : 2·25 : 2·52.

(2) Ampoules made from 150 c.c. Pyrex flasks and extended B19 joints were flamed *in vacuo*, and vanadium tetrachloride and excess of dimethylamine were condensed into them. Dry nitrogen was admitted, to 0·75 atm., to the bulb which was then sealed off at a constriction just beyond the extended ground joint. The contents of the ampoule were allowed to warm to room temperature, shaken mechanically for several hours, and set aside for at least 2 days. The ampoules were then cooled to rather below the b. p. of dimethylamine, scratched with a glass file near the tip, and " hot-spotted "; the tip was removed and the ground joint quickly inserted into a B19 sidearm on the reaction vessel *D* (full of dry nitrogen so that any hydrolysis is negligible), and the contents of the ampoule were tipped into *D*. After the amine had distilled away, the solid was extracted with chlorobenzene; analysis of the product gave: V, 21·8, 21·2; Cl, 33·2, 33·2; N, 14·1, 14·9%; V : Cl : N, 1 : 2·19 : 2·31, 1 : 2·25 : 2·51. Although dimethylammonium chloride is insoluble in chlorobenzene, it seemed likely from the non-stoicheiometric analytical figures that loosely bound amine of the product would modify the solubility,[15] so that traces of the chloride might dissolve in addition to the vanadium compound, and thereby give a product whose overall composition did not correspond to integral

[15] Anderson, *J. Amer. Chem. Soc.*, 1952, **74**, 1421.

V : Cl ratios. In subsequent runs, the loosely held amine was removed by evacuation at 40° for 2 hr. and the product was then extracted as before with chlorobenzene. An analysis of the product gave V : Cl : N = 1 : 2·03 : 1·70, and the molecular weight in nitrobenzene was 260 (a monomer has *M* 197). The departure from integral V : Cl ratios in earlier runs can thus be definitely accounted for by the dissolution of small amounts of dimethylammonium chloride in the chlorobenzene which contained small amounts of free amine, previously loosely associated with the vanadium aminochloride.

Repeating these preparations but extracting each sample several times with chlorobenzene gave products whose V : N ratios approached more closely to 1 : 2 and whose molecular weights were nearer the monomeric value [Found : V : Cl : N, 1 : 2·03 : 1·88; *M*, 227 (required *M*, 206)].

It seems that a small amount of dimer is formed and is almost completely dissolved in the first chlorobenzene washing, and that continued extraction of the same sample then removes monomer, so that the overall composition and molecular weight of the dissolved material get closer to that required by the monomer. Measurements of the magnetic susceptibility of the nitrobenzene solutions gave $\mu = 1{\cdot}62$ B.M., corresponding to one unpaired electron.

A large number of solvents were examined in an attempt to find one which would dissolve either the amine hydrochloride or the vanadium aminochloride but not both. The only ones found were chlorobenzene and nitrobenzene, which dissolved only the aminochloride; chlorobenzene was preferred since it was more readily distilled.

(b) *Vanadium tetrachloride and methylamine.* A vapour-flow preparation was agitated with liquid methylamine at −78°, and then extracted eight times with 100 c.c. of liquid amine; the product of this extraction was then further extracted with chlorobenzene. The chlorobenzene solution was deep red and on evaporation gave a small quantity of a brown-red solid (Found : V : Cl : N, 1 : 2·26 : 2·63). This appears to be $VCl_2(NHMe)_2$ together with a little methylammonium chloride dissolved by the chlorobenzene containing traces of amine.

Next, the reactants, in sealed ampoules, were allowed to react at room temperature; the ampoules were opened [see (a) for details] and the contents extracted with liquid methylamine (6 × 100 c.c.) to remove any methylamine hydrochloride. The solid remaining behind was yellow-green [Found : V, 17·2, 17·6; Cl, 23·3, 23·7; N, 27·7, 27·2. $VCl_2(NHMe)_2,4NH_2Me$ requires V, 17·0; Cl, 23·6; N, 28·0%]. The molecular weight could not be determined since insufficient material dissolved in nitrobenzene; the magnetic susceptibility of the *solid* at room temperature was 1·61 B.M., corresponding to one unpaired electron.

(c) *Vanadium tetrachloride and trimethylamine.* (1) Preliminary experiments were made by condensing the chloride (*ca.* 1 g.) and excess of amine into a tube equipped with a stopcock and ground joint; the tube was detached from the vacuum-line and the contents were allowed to react at 0° (the tube being occasionally shaken), and then the excess of amine was distilled off *in vacuo*. The composition of the reddish-mauve product corresponded to the addition of 1·5—2·0 moles of amine per mole of chloride. When the product was heated by *ca.* 20° intervals to 200°,[16] trimethylamine was steadily lost, together with a small amount of reddish material which sublimed on to the cooler parts of the vessel walls, until the residue had the overall composition VCl_4,NMe_3.

(2) A vapour-flow preparation with the amine at −78° and the chloride–" iso-octane " solution at room temperature gave a buff-coloured product (Found : V, 19·4; Cl, 51·1; N, 6·8%; V : Cl : N, 1 : 3·80 : 1·29). During the preparation, a small amount of almost colourless fine powder was formed above the solution and carried into the outlet tube to the fume chamber. It seems that while the product is largely the adduct VCl_4,NMe_3, a small amount of side reaction occurs giving a replaced body together with the amine hydrochloride (which is found in the outlet tube).

(3) Ampoules of the reactants were prepared and opened in the usual way and after the removal of amine by distillation *in vacuo* the solid remaining was extracted with chlorobenzene; this permanganate-red solution gave a brownish-red solid when the chlorobenzene was evaporated. When this product was heated at 80—100° *in vacuo*, a red crystalline solid sublimed (Found : V, 19·3; Cl, 37·4; N, 10·2%; V : Cl : N, 1 : 2·79 : 1·88). The residue had a similar composition (V, 20·0; Cl, 39·4; N, 10·4%; V : Cl : N, 1 : 2·84 : 1·86). The sublimed crystals were readily hydrolysed in moist air.

With more careful sublimation, carried out by placing the extracted solid in the bottom of a Pyrex vessel containing two constrictions, evacuating the apparatus at the diffusion pump,

[16] Fowles and Pollard, *J.*, 1952, 4938.

sealing it at the upper constriction, and then placing the lower end in a bath at 80—100°, crystals formed in the upper part of the vessel (Found : V, 18·5; Cl, 39·6; N, 10·6. $VCl_3,2NMe_3$ requires V, 18·5; Cl, 38·6; N, 10·4%). Sublimation with direct pumping, or sublimation above 100°, always gave poorly formed crystals (Found : V : Cl : N, 1 : 2·7—2·8 : 1·7—1·8). Later experiments showed that better yields of the initial crude *product* could be obtained if the ampoules of the reactants contained some chlorobenzene; presumably the solvent action of the chlorobenzene prevented the formation of gross surface products and allowed the reaction to take place more readily.

The molecular weight of the sublimate in nitrobenzene was found to be 280 and 254 in successive runs (monomeric $VCl_3,2NMe_3$ requires *M*, 275); after the nitrobenzene solution had been warmed to 40° and evacuated for 1 hr., the molecular weight increased to 356 (in the first instance) while the V : N ratio dropped to 1 : 1·65, showing dimerisation with loss of amine.

The molecular weight of the less clearly defined crystalline product prepared by sublimation at 110—125° was found to be 343.

The magnetic moment, for solutions in chlorobenzene, gave 2·69 and 2·75 B.M., corresponding to two unpaired electrons. The precise nature of the sublimate was confirmed by treating vanadium trichloride with trimethylamine; the reaction was slow, probably because of the difficulty of wetting the chloride, but fair yields of $VCl_3,2NMe_3$ were obtained from the ampoules.

Single crystals were examined by paramagnetic-resonance methods, but no absorption was observed down to the temperature of liquid hydrogen, presumably owing to spin-spin coupling which is commonly found with vanadium compounds. During these studies, the crystals had to be exposed to the atmosphere for some minutes, and to prevent hydrolysis they were covered with a thin film of Silicone oil (previously allowed to stand over phosphoric oxide), and admitted to the crystals *in vacuo*.

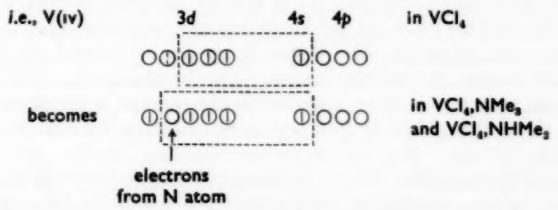
Magnetic Moments.—These were determined at room temperature on a Gouy type balance with a field strength of 8000 gauss.

Molecular Weights.—These were determined cryoscopically under rigorously anhydrous conditions. Temperature changes were recorded on a Beckmann thermometer inserted through a rubber bung (coated with Picein wax, to allow the vessel to be evacuated), and stirring was effected with a stainless-steel spiral agitated through the side of the vessel by an electric motor (connection was made by length of rod fixed with Picein into a pressure-tubing sleeve).

Spectral Measurements.—The absorption spectrum of $VCl_3,2NMe_3$ in chlorobenzene solution shows peaks at 510 and 770 mμ.

Discussion

It seems that the reaction of vanadium tetrachloride with di- and tri-methylamine at low amine concentrations in "iso-octane" solutions gives mainly 1 : 1 adducts $VCl_4,NHMe_2$ and VCl_4,NMe_3, which appear to be thermally stable up to 150° in the absence of free amine. It may be supposed that this adduct is formed by the donation of the lone pair of electrons from the nitrogen atom into a vacant *d* orbital of vanadium, producing a substance of co-ordination number five.



In the diagram, we have assumed that the vanadium atom uses d^3s rather than sp^3 orbitals for the tetrahedral bonds in vanadium tetrachloride, since the 3*d* orbitals are of lower energy that the 4*p*. This leads to the adducts' using d^4s rather than dsp^3 orbitals.

The formation of these 1 : 1 adducts is in agreement with Antler and Laubengayer's finding [9] that the analogous compound $TiCl_4,NMe_3$ is the main product of the corresponding gas-phase reaction.

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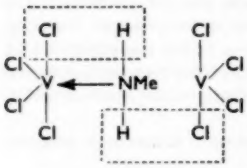
When the dimethylamine concentration is increased, the adduct undergoes a base-catalysed elimination of hydrogen chloride, forming first VCl_3,NMe_2 and finally $VCl_2(NMe_2)_2$. The compound $VCl_2(NMe_2)_2$ is largely monomeric.

The fact that only two of the four chlorine atoms can be replaced by NMe_2 groups is best attributed to the steric difficulty of forming $VCl_2(NMe_2)_2,NHMe_2$ as the necessary intermediate. There is of course no electronic difficulty about forming this compound, because the vanadium atom has the necessary vacant *d* orbital for the formation of the donor–acceptor bond, but once there are two chlorine atoms and two dimethylamino-groups attached to the vanadium atom there will be no space around the vanadium atom to accommodate an extra dimethylamine molecule; the limit appears to be $VCl_3(NMe_2),NHMe_2$, where there is only one amino-group.

On reaction of vanadium tetrachloride with monomethylamine the product $VCl_2(NHMe)_2$ was only very slightly soluble in chlorobenzene and nitrobenzene and insoluble in all other solvents with which it did not react. In view of this very limited solubility, the reaction product is evidently considerably polymerised, which is not of course unexpected since the presence of two hydrogen atoms in the initially co-ordinated amine molecule allows elimination of hydrogen chloride from two neighbouring molecules, and leads to V–NMe–V bridges.



In the analogous reactions of titanic chloride with di- and mono-methylamine, Antler and Laubengayer [9] only studied the room-temperature gas-phase reaction, and they were unable to separate the mixture of products by either vacuum-sublimation or solvents, although the appearance and analysis of these materials agreed with the presence of a mixture of compounds analogous to those we have isolated in the vanadium tetrachloride–amine reactions. These authors showed by chemical tests that a small amount of reduced titanium was present in each product, but we do not find any evidence of vanadium's being reduced to the tervalent state by mono- or di-methylamine.

It seems then, that with both these amines the main product is an aminobasic chloride with two chlorine atoms replaced by amine residues. While only two atoms are replaced in these reactions, the reaction of vanadium tetrachloride with ammonia gives $VCl(NH_2)_3$,[17] showing that the presence of the three hydrogen atoms attached to the nitrogen permits a greater replacement. This can be attributed in part to the greater steric ease with which the ammonia molecule can be co-ordinated, and in part to the greater possibility of elimination of hydrogen chloride.

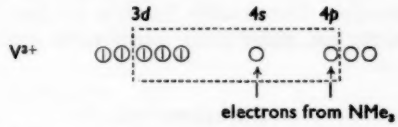
It is not perhaps surprising that reduction takes place in the reaction with trimethylamine since this is a stronger reducing agent than di- or mono-methylamine; a similar reduction in the analogous reaction of titanium tetrachloride and trimethylamine has been observed by Antler and Laubengayer.[9] It is not at all clear, however, just how this reduction takes place, and we have not yet identified any products other than $VCl_3,2NMe_3$ and trimethylammonium chloride; the latter is no doubt formed by the reaction of eliminated acid with excess of trimethylamine. The breaking of a C–H bond which is required if hydrogen chloride is eliminated is in agreement with Meyer and Taube's observations [18] on the splitting out of this acid in the reaction of vanadium tetrachloride with aromatic hydrocarbons. For the titanium reaction, Antler and Laubengayer [9] proposed two possible mechanisms, *viz.*, chlorination of trimethylamine (analogous to the chlorination of pyridine by molybdenum pentachloride proposed by Wardlaw and Webb [19] to account for the reduction of the chloride), and formation of radicals of the type $NMe_2{\cdot}CH_2{\cdot}$. We postpone our discussion until further results are available.

While the exact mechanism of the reduction is unknown, there can be no doubt but

[17] Fowles, unpublished observations.
[18] Meyer and Taube, *Z. anorg. Chem.*, 1935, **222**, 167.
[19] Wardlaw and Webb, *J.*, 1930, 2100.

that the principal product of the reaction of vanadium tetrachloride with excess of trimethylamine at room temperature is $VCl_3,2NMe_3$. The tervalency of vanadium in this complex is confirmed by measurement of its magnetic moment in chlorobenzene solution, which corresponds to two unpaired electrons if we assume the spin-only formula. Molecular-weight measurements show that the substance is monomeric in nitrobenzene solution, so that $VCl_3,2NMe_3$ is a compound in which the vanadium atom has the rather unusual co-ordination number 5. While there is no evidence that this co-ordination remains in the solid state, the ease with which the compound sublimes suggests that it has a low molecular weight. Above 40° in nitrobenzene solution the compound dimerizes with the loss of trimethylamine.

If we accept that 3*d* orbitals will be used for bonding in preference to 4*p* orbitals because of their lower energy, then the most likely arrangement of bonds in $VCl_3,2NMe_3$ is trigonal-bipyramidal with the three chlorine atoms in the planar positions; the vanadium atom would use d^3sp hybrid orbitals, with its two unpaired electrons in the two remaining *d* orbitals.



In a discussion of orbitals used for the alternative arrangements for 5-co-ordination compounds, with particular reference to $VCl_3,2NMe_3$ and $TiCl_3,2NMe$, it has been pointed out [20] that this arrangement would seem more probable than the alternative tetragonal pyramidal one.

Our thanks are expressed to the Department of Scientific and Industrial Research for the award of a maintenance grant (to C. M. P.), to the Chemical Society for a research grant for the purchase of vanadium metal, and to Dr. D. Ingram for the paramagnetic-resonance studies.

UNIVERSITY OF SOUTHAMPTON. [*Received, October 16th*, 1056.]

[20] Fowles and Pleass, *Chem. and Ind.*, 1955, 1743.

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319. *Dinitrogen Trioxide. Part I. Stability in the Gaseous Phase.*

By I. R. BEATTIE and S. W. BELL.

By use of an all-glass apparatus the equilibrium between nitrogen dioxide, dinitrogen tetroxide, nitric oxide, and dinitrogen trioxide has been studied in the gas phase at 5°, 15°, 25°, 35°, and 45°. The equilibrium constant at each temperature has been determined over a wide concentration range, enabling thermodynamic constants to be obtained by extrapolation to zero pressure. Values of $\Delta S°$ and $\Delta H°$ are given.

ALTHOUGH the existence of dinitrogen trioxide has long been assumed very little is known of its properties. It is nevertheless of considerable interest. It has been suggested that it is the active species in *N*-nitrosation and an anticatalyst in nitrations involving the nitronium ion.[1] It is also important in the formation of certain complexes,[2] while the majority of systems containing oxides of nitrogen contain amounts of dinitrogen trioxide

[1] See, *e.g.*, Ingold, "Structure and Mechanism in Organic Chemistry," Bell & Sons Ltd., London, 1953, pp. 284, 398.
[2] Pearson, Henry, Bergmann, and Basolo, *J. Amer. Chem. Soc.*, 1954, **76**, 5920.

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dependent on both the temperature and the composition of the mixture. Several investigators have studied dinitrogen trioxide, although the range of stability of the pure compound is not known. Lipscomb and Reed's [3] *X*-ray analyses did not yield a satisfactory structure.

Abel and Proisl,[4] using Bodenstein's values [5] for the dinitrogen tetroxide–nitrogen dioxide equilibrium, evaluated the equilibrium constant for the reaction (1) over a wide

$$N_2O_3 \rightleftharpoons NO + NO_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

concentration range at several different temperatures. Extrapolation to zero pressure gave the values at 8·13° and 34·8° as 0·539 and 2·39 atm. respectively. The results yield a value for the heat of reaction of 9600 cal. mole^{-1} (a fuller account which was to have been given in *Z. phys. Chem.* did not appear). Insufficient data are given [4] to plot the results in the manner now to be described. Verhoek and Daniels [6] studied the equilibrium (1), but the equilibrium constants they obtained (2·105 at 25°, 3·673 at 35°, and 6·880 atm. at 45°; $\Delta H°$ 10,300 cal. mole^{-1}) differed considerably from those of Abel and Proisl.

In view of the considerable discrepancies between the two sets of observations, and since the equilibrium in the gas phase is of considerable analytical importance, it was decided to reinvestigate it.

Experimental

All work was carried out in a vacuum system.

Nitric Oxide.—This was prepared as described by Johnston and Giauque,[7] except that the theoretical quantities of potassium nitrite and potassium iodide were used. The first and the last portion of each distillate from the original material were rejected. Johnston and Giauque reported that they obtained a blue liquid, while Nightingale *et al.*[8] have recently stated that the colour of their product was pale straw-green. We obtained apparently colourless nitric oxide.

Nitrogen Dioxide.—" AnalaR " lead nitrate which had been dried for several days at 200—250° was heated at this temperature *in vacuo*. On raising the temperature to approximately 340° gases were collected in a trap cooled in solid carbon dioxide after passage through a phosphoric oxide column. The product was distilled in an atmosphere of oxygen. After removal of the oxygen the mixture was again distilled, the first and the last fraction being rejected.

An accurately weighed ampoule was partially filled by distillation, sealed, and separated at a previously made constriction. After rigorous cleaning the ampoule was reweighed. This technique was checked several times by using no nitrogen dioxide. The results indicated a high order of reproducibility for the weighings if a standard method of treatment was followed exactly. All joints were carefully greased with I.C.I. " Florube " W grease, so that a minimum quantity came into contact with the nitrogen dioxide.

Apparatus and Technique.—An all-glass apparatus was used as we found that all possible greases either reacted with or absorbed oxides of nitrogen during the experiment. Fluorinated greases appear to be unreactive, but extensive physical sorption occurs. The reaction vessel, *A*, and pressure measuring system are shown in Fig. 1. An ampoule containing nitrogen dioxide was introduced into the internally calibrated tube *B*, together with a steel-in-glass breaker. Tube *B* was subsequently joined to the vacuum line *via* a constriction *C*. The apparatus was continuously pumped for at least 2 days, since it was impracticable to flame out the glassware. By surrounding the projection *D* with liquid air a quantity of nitric oxide could be distilled into the reaction system. The constriction at *C* was sealed after pumping on the nitric oxide for a short while. The nitric oxide was allowed to attain a steady temperature, the pressure was noted, and the nitrogen dioxide ampoule broken. Complete mixing of the gases was ensured by successively freezing them out in *D*, followed by leaving the mixture

[3] Lipscomb and Reed, *Acta Cryst.*, 1953, **6**, 781.
[4] Abel and Proisl, *Z. Elektrochem.*, 1929, **35**, 712.
[5] Bodenstein, *Z. phys. Chem.*, 1922, **100**, 68.
[6] Verhoek and Daniels, *J. Amer. Chem. Soc.*, 1931, **53**, 1250.
[7] Johnston and Giauque, *J. Amer. Chem. Soc.*, 1929, **51**, 3194.
[8] Nightingale, Downie, Rotenberg, Crawford, and Ogg, *J. Phys. Chem.*, 1954, **58**, 1047.

for at least two days to come to equilibrium. Pressures were then measured at temperatures near 5°, 15°, 25°, 35°, and 45°. At the end of the experiment the tube *B* was cut squarely in the undistorted portion just below *C*, the distance from a reference point to the cut being noted. The volume of the removed cup, the ampoule, and the magnetic breaker was measured. The internal volume of the main apparatus (at least 1 l.) was eventually found up to the same reference point in *B*.

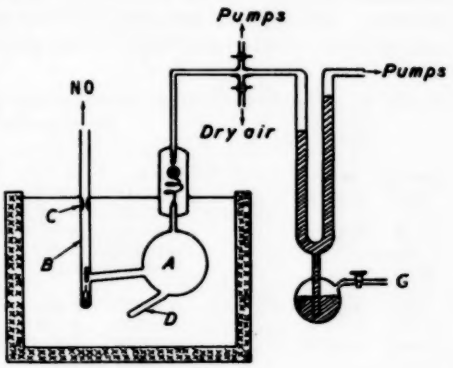

FIG. 1.

Pressures were measured by using a sensitive spiral gauge with a 3-metre optical beam as a null instrument. The double-tube mercury manometer, having a common reservoir, was constructed of Chance's "Veridea" tubing (1·6 cm. internal diam.). The pressure on the spiral gauge was varied by the introduction of dry air, fine adjustment being possible by means of tap G. Pressure readings are expressed in international atmospheres and are accurate to $\pm 5 \times 10^{-5}$ international atmospheres. All weighings were carried out with calibrated weights, and the thermometers were standardised against a previously calibrated ten-junction copper–constantan thermocouple.

DISCUSSION

In a mixture containing only nitrogen dioxide, dinitrogen tetroxide, nitric oxide, and dinitrogen trioxide, equations (2—5) are valid for ideal gases, where p (with symbol in parentheses) is the partial pressure at equilibrium, p^0 is the initial partial pressure [$p^0(N_2O_4)$, no dissociation being assumed], and P = the total pressure at equilibrium.

$$K_1 = p^2(NO_2)/p(N_2O_4) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$p^0(NO) = p(NO) + p(N_2O_3) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$2p^0(N_2O_4) = 2p(N_2O_4) + p(NO_2) + p(N_2O_3) \quad . \quad . \quad . \quad . \quad (4)$$

$$P = p(N_2O_4) + p(NO_2) + p(NO) + p(N_2O_3) \quad . \quad . \quad . \quad . \quad (5)$$

From eqns. (5) and (4), $2p(NO) = 2P - 2p^0(N_2O_4) - p(NO_2) - p(N_2O_3)$

which with eqn. (3) yields $p(NO) = 2P - 2p^0(N_2O_4) - p(NO_2) - p^0(NO)$ (6) (cf. ref. 6)

From eqns. (5), (3), and (2), $p^2(NO_2) + K_1p(NO_2) + K_1[p^0(NO) - P] = 0 \quad . \quad . \quad (7)$

Whence for real roots $p(NO_2) = \frac{1}{2}(-K_1 + \sqrt{\{K_1^2 + 4K_1[P - p^0(NO)]\}})$

Clearly from (3), (6), and (7) it is possible to evaluate K_2 where

$$K_2 = p(NO) \cdot p(NO_2)/p(N_2O_3)$$

A reaction involving dinitrogen tetroxide would yield an equilibrium constant $K_3 = K_2^2/K_1$ and K_3 and K_2 would presumably each have a different dependence on concentration, as pointed out by Verhoek and Daniels. With the two equilibria involved this does not appear to be relevant to the problem.

It is extremely unlikely that any molecular species other than NO, NO_2, N_2O_3, and N_2O_4 is present at equilibrium. This does not exclude the possibility of the presence of structural isomers for N_2O_3 and N_2O_4, although these would not markedly affect the pressure dependence of the results.

The experimental results are given in Table 1 [data for the nitrogen dioxide–dinitrogen

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tetroxide equilibrium were calculated from the material and by the method recommended by Giauque and Kemp [9]. It is evident that quite wide variations occur in K_2. These deviations may be due to non-ideality of the gases, sorption, or variations in K_1 with pressure. Although the amount of gas sorbed on the walls of the vessel necessary to form a monolayer would cause errors in the pressure readings only within the experimental

TABLE 1. *Experimental observations on the dinitrogen trioxide equilibrium and calculated equilibrium constants.*

Temp.	A * (atm.)	Vol. (ml.) †	P (atm.)	K_2 (atm.)	Temp.	A * (atm.)	Vol. (ml.) †	P (atm.)	K_2 (atm.)
4·96°	1·48728	1265·5	0·58548	0·374	5·00°	0·50110	1269·1	0·44680	0·478
15·00		(1268·3)	0·63033	0·752	15·01		(1271·9)	0·47492	0·909
25·04	(0·30129)		0·68017	1·34	25·12	(0·36709)		0·50559	1·66
35·08			0·73626	2·29	35·02			0·53658	2·71
45·12			0·79774	3·83	45·10			0·56892	4·48
4·96	1·21744	1263·8	0·56971	0·409	15·00	2·10492	1272·1	0·60501	0·606
15·00		(1266·9)	0·61060	0·776	24·97	(0·12580)	(1274·5)	0·65907	1·12
25·04	(0·34391)		0·65754	1·43	35·01			0·72206	1·95
35·08			0·70769	2·30	45·01			0·79228	3·23
45·12			0·76315	3·76					
4·96	0·84238	1264·5	0·24187	0·435	4·95	1·34501	1273·1	0·34848	0·353
15·00		(1267·6)	0·26480	0·759	14·92		(1275·5)	0·37960	0·692
25·04	(0·05488)		0·29187	1·52	24·96	(0·05856)		0·41736	1·29
					35·12			0·46101	2·26
4·96	0·47498	1271·5	0·67870	0·457	45·12			0·50843	3·79
15·00		(1274·5)	0·71589	0·869					
25·04	(0·63231)		0·75555	1·59	4·95	1·33390	1270·7	0·72332	0·417
35·08			0·79579	2·65	14·97		(1273·1)	0·77215	0·799
45·12			0·83678	4·60	25·04	(0·49548)		0·82707	1·46
					34·99			0·88559	2·41
5·03	0·53386	1269·2	0·63475	0·476	45·04			0·94984	3·94
15·08		(1272·4)	0·67120	0·911					
25·07	(0·56959)		0·70951	1·61	15·00	2·10885	1271·6	0·83070	0·655
35·11			0·74995	2·77	25·01	(0·38256)	(1274·2)	0·89544	1·19
45·19			0·79087	4·52	35·07			0·96888	2·06
5·05	0·45360	1268·4	0·71440	0·463					
15·03		(1271·4)	0·75387	0·952	14·95	2·22996	1270·9	0·85894	0·670
25·07	(0·67577)		0·79364	1·68	25·04	(0·38471)	(1273·3)	0·92652	1·24
35·04			0·83449	2·77	35·05			1·00249	2·16
45·21			0·87689	4·62					
5·01	0·87667	1268·0	0·79707	0·427	4·99	0·52400	1268·1	0·43329	0·471
15·01		(1271·0)	0·84459	0·819	15·00		(1270·4)	0·46101	0·883
25·07	(0·67986)		0·89641	1·49	25·04	(0·34674)		0·49133	1·59
35·08			0·45055	2·49	35·16			0·52313	2·65
45·08			1·00728	4·04	45·05			0·55526	4·49
4·86	0·08535	1268·6	0·26347	0·590	4·86	0·97346	1268·3	0·63796	0·427
15·01		(1270·1)	0·27587	0·921	14·95		(1270·7)	0·68003	0·815
25·04	(0·26059)		0·28880	1·83	25·04	(0·47831)		0·72638	1·48
35·08			0·30098	3·03	35·02			0·77586	2·46
45·12			0·31274	5·12	45·21			0·82918	4·03

* A, Mass of N_2O_4 (g.) with the measured pressure of NO at the temperature nearest 25° in parentheses.

† Vol. of cell containing NO, with vol. of cell containing the equilibrium mixture in parentheses.

error, it is possible that the sorbed gases, by affecting the surface of the glass in the spiral, could cause errors in the zero readings of the gauge. The deviations mentioned would be removed on extrapolation to zero pressure. The sorption of the polar molecule NO_2 is likely to be higher than that of any other species present. The results were therefore plotted for K_2 as a function of the partial pressure of nitrogen dioxide, and are shown in Fig. 2. The

[9] Giauque and Kemp., *J. Chem. Phys.*, 1938, **6**, 40.

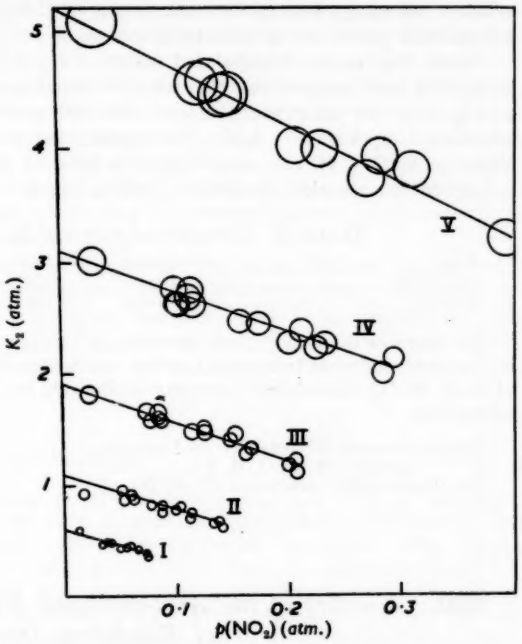

FIG. 2. *Equilibrium constant for the dissociation of dinitrogen trioxide as a function of the partial pressure of the nitrogen dioxide.*

I, 5°; II, 15°; III, 25°; IV, 35°; V, 45°.

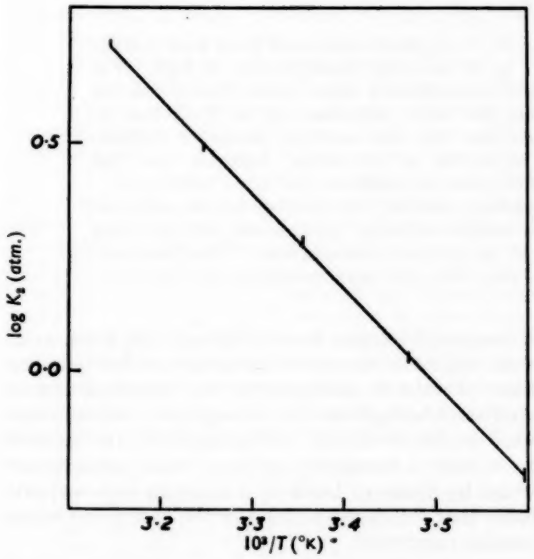

FIG. 3. *The relation between the logarithm of the extrapolated equilibrium constant for the dissociation of dinitrogen trioxide and the reciprocal of the absolute temperature.*

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circles represent errors of ±4% from the centre. It is probable that there is a linear relation, all except four of the circles being on the lines which have been drawn (2 of these exceptional points are at extremely low pressures).

Table 2 gives the extrapolated values of K_2 at various temperatures (obtained by the method of least squares) together with the standard deviation σ. These results are plotted in Fig. 3, giving the expected linear relationship between log K_2 and the reciprocal of the absolute temperature. Again, the application of the least-squares method yielded a value of 9527 ± 96 cal. mole^{-1} for the heat of reaction. The corresponding entropy change for the reaction was 33·25 ± 0·35 cal. mole^{-1} deg.$^{-1}$.

TABLE 2. *Extrapolated values of K_2 at various temperatures.*

Temp.	45·00°	35·00°	25·00°	15·00°	5·00°
$K_2°$ (atm.)	5·193	3·097	1·916	1·082	0·595
σ (atm.)	±0·059	±0·041	±0·027	±0·025	±0·018

The authors thank Mr. York for two spiral guages. Various greases were kindly supplied by Imperial Chemical Industries Limited and Messrs. Halocarbon Products Corporation. One of us (S. W. B.) thanks the University of Sheffield for a Robert Styring postgraduate research scholarship.

KING'S COLLEGE (UNIVERSITY OF LONDON),
LONDON, W.C.2 (I. R. B.).
THE UNIVERSITY, SHEFFIELD (S. W. B.). [*Received, November 2nd,* 1956.]

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320. *Kinetics of the Acid-catalysed Hydrolysis and Decomposition of Ethylidene Diacetate.*

By R. P. BELL and B. LUKIANENKO.

The kinetics of the hydrolysis of ethylidene diacetate have been studied in aqueous hydrochloric acid up to an acid concentration of 8·9M. The reaction velocity follows the acid concentration more closely than it does the acidity function, thus showing the same behaviour as the hydrolysis of simple esters. It is concluded that the two reactions proceed by similar mechanisms, and that the hydrolysis of ethylidene diacetate does not involve preliminary decomposition into acetaldehyde and acetic anhydride.

The decomposition of ethylidene diacetate in chlorobenzene is catalysed by trichloroacetic acid and by stannic chloride, the reaction velocity being proportional to the first power of the catalyst concentration. Under the same conditions stannic chloride is more effective than trichloroacetic acid by a factor of about 15,000.

ETHYLIDENE DIACETATE is hydrolysed in aqueous solution to acetaldehyde and acetic acid, the reaction being of the first order with respect to the ester, and catalysed by hydrogen ions and hydroxyl ions.[1] In the absence of water it undergoes thermal decomposition in the range 200—300° to acetaldehyde and acetic anhydride by a homogeneous unimolecular gas reaction.[2] Bell and Burnett[3] were unable to detect acid catalysis in the gaseous decomposition; however, ethylidene diacetate is commonly prepared from acetaldehyde and acetic anhydride at low temperatures by means of Lewis-acid catalysts such as ferric bromide, and it therefore seems probable that the decomposition in the absence of water will also exhibit acid catalysis under suitable conditions.

The above behaviour resembles that of the structurally similar paraldehyde, which

[1] Skrabal, *Z. phys. Chem.*, 1926, **122**, 357; 1927, **128**, 457.
[2] Coffin, *Canad. J. Res.*, 1932, **7**, 75.
[3] Bell and Burnett, *Trans. Faraday Soc.*, 1939, **35**, 474.

decomposes to acetaldehyde by a homogeneous gas reaction,[4,5] by an acid-catalysed heterogeneous gas reaction,[6] and by an acid-catalysed homogeneous reaction both in water [7] and in non-aqueous solvents.[8,9] In concentrated aqueous solutions of acids the rate of depolymerisation of paraldehyde is more closely parallel to the acidity function than to the hydrogen-ion concentration, and this may be regarded as evidence that (even in aqueous solution) the rate-determining step does not involve a water molecule : [7] the same is true of the hydrolysis of dimethoxymethane.[10] The hydrolysis of ethylidene diacetate might follow a similar course : on the other hand, it also resembles the simple carboxylic esters, for which the rate of acid hydrolysis follows the acid concentration rather than the acidity function,[11] thus supporting the generally accepted mechanism [12] with a water molecule in the transition state.

Skrabal's measurements [1] on the acid hydrolysis of ethylidene diacetate extend only up to 1M-acid, at which concentration there is little difference between the acidity function and the hydrogen-ion concentration. We have therefore made measurements in the range 0·3—9M-aqueous hydrochloric acid, and have also investigated briefly the acid-catalysed decomposition in chlorobenzene.

Experimental

Ethylidene diacetate was a commercial sample containing less than 0·1% of free acetaldehyde. Its purity was estimated as 95—97% by complete hydrolysis to acetaldehyde and titration of the latter as described below. The remaining 3—5% was shown to be mainly acetic anhydride by hydrolysing it in neutral solution (which does not affect the ester) and titrating the acetic acid with sodium hydroxide. Attempts to purify the ester by distillation produced no improvement (probably because of further thermal decomposition), and since it was shown later that the addition of acetic anhydride had no effect on the kinetics the original sample was used without purification. Hydrochloric acid, trichloroacetic acid, and stannic chloride were " AnalaR " products, the first being standardised against recrystallised borax. Chlorobenzene was dried ($CaCl_2$ then P_2O_5) and distilled.

In all the kinetic measurements the acetaldehyde produced was estimated by Friedemann, Cotonio, and Shaffer's method.[13] For the measurements in aqueous solution 50 c.c. of solution 0·02—0·03M in ester were kept at 25° and at intervals a 2 c.c. sample was run into 5 c.c. of 0·2M-sodium hydrogen sulphite solution. After 15 min. most of the excess of hydrogen sulphite was removed with 0·25N-iodine solution, and the remainder by titration with 0·015N-iodine solution (starch). The aldehyde–bisulphite compound was then decomposed by adding 1 g. of solid sodium hydrogen carbonate, and the hydrogen sulphite liberated titrated with 0·015N-iodine solution. At the higher acid concentrations (>4·0M) it was necessary to neutralise some of the acid in the sample by adding sodium hydroxide (and ice) to the sodium hydrogen sulphite solution.

In aqueous hydrochloric acid the hydrolysis was kinetically of the first order during 90% of its course, and the velocity constants were determined graphically by plotting log $(C_\infty - C_t)$ against t, where C_t is the concentration of acetaldehyde after time t. The value of C_∞ was calculated from the weight of ester taken. The velocity constants are collected in Table 1.

Catalysis in non-aqueous solution was studied in less detail, the object being to establish the general character of the decomposition under these conditions. The analytical method used for following the reaction was the same as for aqueous solutions. For each catalyst concentration a number of samples were sealed in glass bulbs, and analysed at intervals.

[4] Coffin, *Canad. J. Res.*, 1931, **5**, 636.
[5] Bell and Burnett, *Trans. Faraday Soc.*, 1938, **34**, 420.
[6] *Idem, ibid.*, 1937, **33**, 355.
[7] Bell and Brown, *J.*, 1954, 774.
[8] Bell, Lidwell, and Vaughan-Jackson, *J.*, 1936, 1792.
[9] Bell and Skinner, *J.*, 1952, 2955.
[10] McIntyre and Long, *J. Amer. Chem. Soc.*, 1954, **76**, 3240.
[11] Bell, Dowding, and Noble, *J.*, 1955, 3106.
[12] Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686.
[13] Friedemann, Cotonio, and Shaffer, *J. Biol. Chem.*, 1927, **73**, 342.

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Catalysis by trichloroacetic acid in chlorobenzene was studied at 100°, and in preliminary experiments the reaction velocity was found to fall off with time more rapidly than corresponded to a first-order reaction. Tests showed that this behaviour was not primarily due to reversibility of the decomposition or to polymerisation of the acetaldehyde produced, but could be attributed mainly to the reaction $(CH_3{\cdot}CO)_2O + 2CCl_3{\cdot}CO_2H \longrightarrow (CCl_3{\cdot}CO)_2O + 2CH_3{\cdot}CO_2H$, which replaces the trichloroacetic acid by the much less effective acetic acid. Thus if a trichloroacetic acid solution was heated to 100° with an equivalent amount of acetic anhydride before use its catalytic power was found to be greatly diminished. In order to minimise this complication a low concentration of ester was used (<0·01M) and only the first 50% of each reaction was followed: the velocity constants given in Table 2 are therefore less accurate than those for aqueous solutions.

TABLE 1. *Hydrolysis of ethylidene diacetate in aqueous hydrochloric acid at* 25°.

c = acid concn. (M) *; k = first-order velocity constant (sec.$^{-1}$).

c	0·330	0·391	0·489	0·713	1·129	1·614	2·26	3·39
H_0	0·44	0·38	0·28	0·11	−0·14	−0·40	−0·63	−1·04
10^5k	3·58	4·50	5·43	7·58	11·5	19·5	30·5	54·2
c	4·51	4·52	6·54	8·08	8·28	8·73	8·88	
H_0	−1·46	−1·46	−2·26	−2·89	−2·96	−3·12	−3·14	
10^5k	87·2	82·3	145	221	277	356	333	

TABLE 2. *Decomposition of ethylidene diacetate in chlorobenzene.*

c = catalyst concn. (M); k = first-order velocity constant (sec.$^{-1}$).

(*a*) Solutions of trichloroacetic acid at 100°.

c	0·0874	0·133	0·205	0·375	0·417	0·457	0·692	1·04
10^5k	1·1	1·2	2·1	3·9	4·4	5·2	9·3	19

(*b*) Solutions of stannic chloride at 25°.

c	0·00529	0·00821	0·0181	0·0199	0·0266	0·0314	0·0407	0·0417
10^5k	2·5	8·1	21	23	29	30	45	46

Dilute solutions of stannic chloride in chlorobenzene were found to decompose the ester rapidly at 25°. (The presence of the stannous–stannic redox system made it necessary to modify the method of analysis as described by Bell and Skinner.[9]) There were again considerable departures from first-order behaviour, in this case probably because the decomposition is appreciably reversible under these conditions. The results given in Table 2 were obtained by using dilute ester solutions (<0·01M) and correspond to the first 20—30% of the reaction.

DISCUSSION

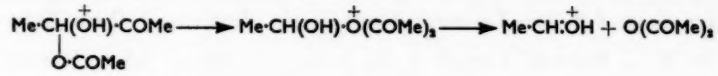
The results in aqueous hydrochloric acid (Table 1) lead to the most definite conclusions about the mechanism of the reaction. The Figure shows a plot of $\log_{10}k$ against H_0 or $\log_{10}c$, the values of H_0 being taken from Hammett's measurements [14] as extended by Bell, Dowding, and Noble.[11] The straight line is drawn with unit slope. It is clear that the relation to H_0 is far from linear, while the curve relating $\log_{10}k$ to $\log_{10}c$ has an upward curvature closely resembling that found for the hydrolysis of simple esters.[11] (This curvature is diminished if the concentration is expressed in moles per kg. of solvent rather than per litre of solution.) This is good evidence that the hydrolysis of ethylidene diacetate in aqueous solution proceeds by the same mechanism as the hydrolysis of simple esters, and does not involve a slow decomposition into acetaldehyde and acetic anhydride followed by rapid hydration of the latter.

The results in chlorobenzene solution (Table 2) show that the decomposition is catalysed both by proton acids and by Lewis acids. The function of the acid catalyst may be to lower the activation energy needed for the electronic rearrangement involved (by giving a

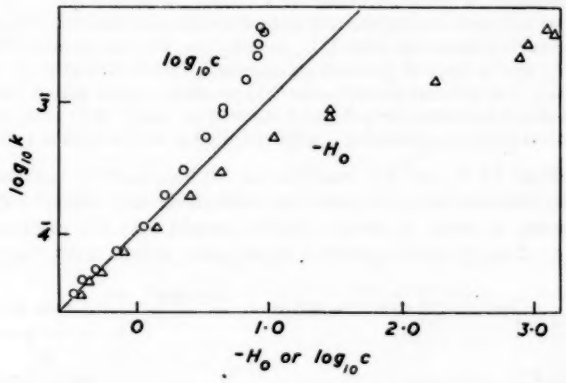
* Throughout this paper we emphasise that M (molar) has its usual meaning of moles of solute per litre of solution (see *J.*, 1955, 4498).

[14] Hammett and Paul, *J. Amer. Chem. Soc.*, 1934, **56**, 830.

positive charge to one of the acyl oxygen atoms) : alternatively, it is possible to formulate a mechanism in two steps,



which is closely analogous to that suggested for the decomposition of paraldehyde.[7] Table 2 shows that for the reaction studied here the velocity is proportional to the first power of the acid concentration, in contrast with the power of approximately two found



for the decomposition of paraldehyde in non-aqueous solvents.[8,9] The difference probably depends on the fact that the paraldehyde molecule contains three equivalent oxygen atoms, and that the most efficient mode of decomposition involves the attack on two of them by catalyst molecules.

The results in Table 2 do not permit any direct comparison of the catalytic powers of trichloroacetic acid and stannic chloride because of the difference in temperature. Two experiments with trichloroacetic acid at 25° gave an approximate value of $k = 9 \times 10^{-7}$ sec.$^{-1}$ for a 1M-catalyst concentration, showing that stannic chloride is about 15,000 times more effective than trichloroacetic acid : this resembles the behaviour of Lewis acids and proton acids in the decomposition of paraldehyde.[9] By combining the velocity constants for trichloroacetic acid at 25° and 100° we find $E \simeq 18$ kcal./mole, $A \simeq 10^7$ l. mole^{-1} sec.$^{-1}$ for the parameters of the Arrhenius equation. The value of A is less than the collision-theory value by a factor of about 10^4, as is commonly found for reactions between uncharged molecules which proceed by an ionic mechanism.

PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, November 8th,* 1956.]

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321. β-*Aroylpropionic Acids. Part VII.* The Action of Grignard Reagents on Succinic Anhydride, Methylsuccinic Anhydride, and* β-*Aroyl- and* β-*Aroyl-*α-*methyl-propionic Acids and their Esters.*

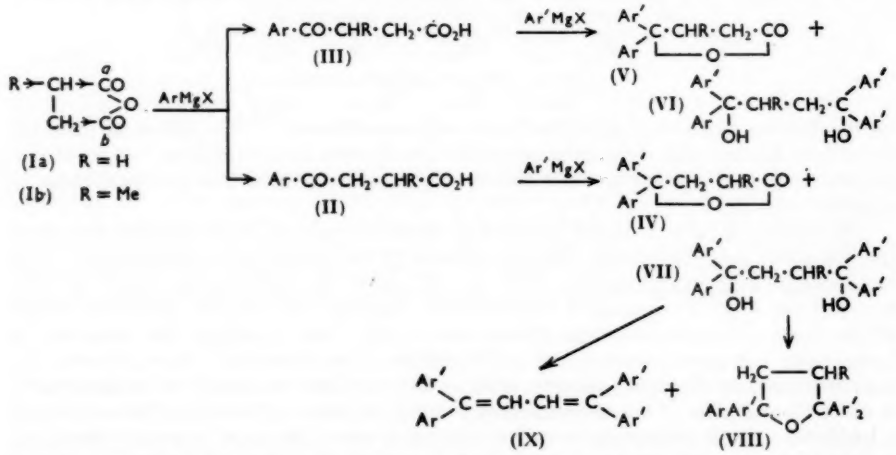
By F. G. Baddar, Lanson S. El-Assal, and (Mrs.) Adiba Habashi.

Arylmagnesium halides with succinic anhydride give β-aroylpropionic (II) and γγ-diaryl-γ-hydroxybutyric acid, isolated as its lactone (IV), and a neutral product from which a tetrahydrofuran (VIII) is isolated. When β-aroylpropionic acids were used instead of succinic anhydride, the neutral product contained a tetrahydrofuran or a buta-1 : 3-diene (IX).

The reaction with methylsuccinic anhydride gives a mixture of β-aroyl-α- (II) and -β-methylpropionic acid (III), γγ-diaryl-α- (IV) and -β-methylbutyrolactone (V), and a neutral product containing a tetrahydrofuran (VIII).

However, β-aroyl- and β-aroyl-α-methyl-propionic esters give 3 : 3-diaryl- and 3 : 3-diaryl-1-methyl-prop-2-ene-1-carboxylic acid (XI), respectively, with a neutral product containing a tetrahydrofuran and/or a buta-1 : 3-diene.

Previous work (Part IV*) on the reaction of arylmagnesium halides with succinic anhydride has been extended to methylsuccinic anhydride and β-aroyl-α-methylpropionic acids and their esters, in order to obtain further insight into the mechanism. 2 : 5-Dimethoxyphenyl- or 2-methoxy-1-naphthyl-magnesium iodide with succinic anhydride



gave a mixture of the β-aroylpropionic acid (II; R = H) and γγ-diaryl-γ-hydroxybutyric acid, isolated as its lactone (IV; R = H). In the former case a neutral product was also obtained, from which the furan (VIII; R = H) was isolated. However, with methylsuccinic anhydride phenyl-, *p*-tolyl-, *p*-methoxyphenyl-, α-naphthyl-, *o*-methoxyphenyl-, or 2 : 5-dimethoxyphenyl-magnesium halide gave β-aroyl-α- (II; R = Me) and -β-methylpropionic acid (III; R = Me) and γγ-diaryl-α- (IV; R = Me) and -β-methylbutyrolactone (V; R = Me). In the last two cases both lactones were obtained pure, together with a tetrahydrofuran (VIII; R = Me). However, in the other cases either an inseparable mixture of lactones or the α-methyl lactone only was obtained; no tetrahydrofuran or buta-1 : 3-diene was isolated from the neutral fraction (see Tables). The structure of the α-methylbutyrolactone (IV; R = Me) was established by its identity with the product obtained by the action of Grignard reagent on the corresponding β-aroyl-α-methylpropionic acid (II; R = Me).

* Parts IV–VI, *J.*, 1955, 456, 2199, 4469.

However, when β-aroyl- or β-aroyl-α-methyl-propionic esters were used, 3 : 3-diaryl- (XI; R = H) or 3 : 3-diaryl-1-methylprop-2-ene-1-carboxylic acids (XI; R = Me) were obtained instead of the corresponding lactones (IV; R = H and Me, respectively).

TABLE 1. *Reactions of Grignard compounds* ArMgX (2 *mols.*) *with succinic* (Ia) *or methylsuccinic anhydride* (Ib).

	Yields * (%) of products					
Ar	(II)	(III)	(IV)	(V)	(VIII)	(IX)
Anhydride (Ia)						
2 : 5-$(MeO)_2C_6H_3$	25·2		25·1		0·7	
2 : 1-MeO·$C_{10}H_6$	31		1·1			
,, (1 mol.)	31					
Anhydride (Ib)						
Ph	11·8 [a]	2·5 [a]	4·2			
p-C_6H_4Me	9·6 [a]	3·7 [a]	1·1			
o-MeO·C_6H_4	3·4	1·4	5·4 [a]	1·5	6·0	
,, (1 mol.)	5·5	2·1	6·3 [a]	1·5	←Oil→	
2 : 5-$(MeO)_2C_6H_3$	3·0 [a]	10·9 [b]	4·4 [a]	1·2	2·2	
p-MeO·C_6H_4	2·7 [a]	8·9 [b]	←7·3→ [c]		←?→ [c]	
1-$C_{10}H_7$	9·4 [a]	15·7 [b]	2·2			

* Yields are calculated on the crude product unless stated as (*a*) pure product, (*b*) oil, or (*c*) semi-solid.

TABLE 2. *Reactions of Grignard compounds* Ar'MgX (2 *mols.*) *with* β-*aroylpropionic acids* (II) *or* (III) *or their esters* (X).

			Reactant	Yields * (%) of products					
Ar'		R	Ar	(II) [d]	(IV)	(V)	(VIII)	(IX)	(XI)
2 : 5-$(MeO)_2C_6H_3$	II	H	2 : 5-$(MeO)_2C_6H_3$	56 [d]	9·0		2·3		
o-MeO·C_6H_4	II	H	,,	52 [d]	Trace		←(VIIa)→		
,,	II	H	2 : 1-MeO·$C_{10}H_6$	64 [d]				2·0	
,,	II	H	2 : 5-MeO·C_6H_3Ph	48 [d]	6·1		←Mixed→		
,,	II	H	A †	70 [d]	4·9		4·6		
,,	II	H	2 : 5-MeO·C_6H_3Me	76 [d]	8·6		3·5		
,,	II	H	2 : 5-MeO·C_6H_3Cl	64 [d]	5·8		5·5		
,,	II	Me	*o*-MeO·C_6H_4	30 [d]	18·6		←Trace→		
2 : 5-$(MeO)_2C_6H_3$	II	Me	2 : 5-$(MeO)_2C_6H_3$	66	10·8				
Ph	II	Me	Ph	34	10·0				
p-C_6H_4Me	II	Me	*p*-C_6H_4Me	56	8·8				
,,	III	Me	,,	36		11·8 [b]			
p-MeO·C_6H_4	II	Me	*p*-MeO·C_6H_4	46	4·7		←?→		
1-$C_{10}H_7$	II	Me	1-$C_{10}H_7$	60	3·4				
2 : 5-$(MeO)_2C_6H_3$	X	H	2 : 5-$(MeO)_2C_6H_3$				3·2		16·5
o-MeO·C_6H_4	X	H	2 : 5-MeO·C_6H_3Ph				←Mixture→		15·8
,,	X	H	2 : 5-MeO·C_6H_3Me				0·8	3·2	
,, (1 mol.)	X	H	,,				1·6		18·1
,,	X	H	2 : 5-MeO·C_6H_3Cl				4·6		19·2
Ph	X	Me	Ph				←Mixed→		16·4
2 : 5-$(MeO)_2C_6H_3$	X	Me	2 : 5-$(MeO)_2C_6H_3$				4·9		21·4

* Cf. Table 1; (*d*) Recovered. † 2 : 5-$(MeO)_2C_6H_3$·C_6H_4·OMe-*p*.

The isomerisation of γγ-di-*o*-methoxyphenyl-α-methyl-, γγ-di-2 : 5-dimethoxyphenyl-, and γγ-di-2 : 5-dimethoxyphenyl-α-methyl-butyrolactone with boiling concentrated hydrochloric acid [1] gave the corresponding 3 : 3-diarylprop-2-ene-1-carboxylic acids (XI), identical

$$\underset{(X)}{Ar\cdot CO\cdot CH_2\cdot CHR\cdot CO_2Me} \xrightarrow{Ar'MgX} HO\cdot CArAr'\cdot CHR\cdot CO_2Me \longrightarrow \underset{(XI)}{ArAr'C{=}CH\cdot CHR\cdot CO_2H}$$

with those obtained from the esters. The structures of the propene acids, 1 : 1 : 4 : 4-tetra-arylbutadienes, and 2 : 2 : 5 : 5-tetra-aryltetrahydrofurans were confirmed by their absorption spectra (see following paper).

Geometrical isomerism is possible among the buta-1 : 3-dienes and propene acids in

[1] Baddar and El-Assal, *J.*, 1951, 431.

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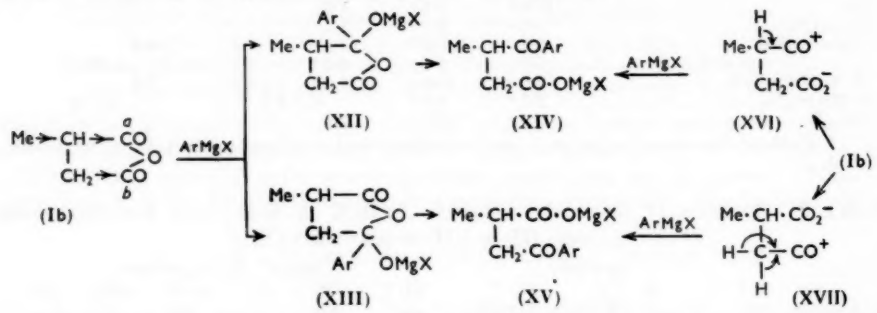
which Ar and Ar' are not identical, but the configurations of the products now described cannot at present be determined.

The results (see Table) show that the highest yields of lactones and furans or butadienes are obtained when *o*-methoxyphenylmagnesium halide reacts with a β-*o*-methoxyaroylpropionic acid. This confirms Baddar and El-Assal's previous assumption.[1]

The non-reactivity of β-2-methoxy-1-naphthoylpropionic acid towards Grignard reagents (see Table) may be due to steric factors, caused by the additional ring,[2] which inhibits formation of the co-ordination complex.[1]

The formation of the α-methyl-acids (II; R = Me) and the α-methyl-lactones (IV; R = Me) in greater proportion than the β-methyl-isomers (III and V; R = Me, respectively) could be attributed either to steric [2,3] or to polar factors. Steric effects may be the main factor operating with bulky groups, such as phenyl.[3a]



Thus, if the reaction takes place by addition to the carbonyl group,[4] then carbon atom (*b*) will be more deficient in electrons than carbon atom (*a*), and, therefore, the Grignard reagent will add preferentially to the former, to give (XV). However, if the reaction takes place by the opening of the anhydride ring,[5] to give the two ions (XVI) and (XVII), then ion (XVII) will be formed to a greater extent, owing to hyperconjugation, leading to the predominant formation of the α-methyl-acid. Whether the methyl group operates by a steric or a polar effect is left for further investigation.

Experimental

β-2 : 5-*Dimethoxybenzoyl-α-methylpropionic Acid.*—(i) A solution of ω-bromo-2 : 5-dimethoxyacetophenone [6] (5·4 g.) in dry benzene (30 ml.) was gradually added to a mixture of sodium ethoxide (from 0·5 g. of sodium in 12·5 ml. of alcohol) and methyl malonate (3·8 g.), and the mixture was worked up as described by Mayer and Stamm.[7] The product was hydrolysed with 5% alcoholic potassium hydroxide (1·5 hours' refluxing), and the resulting acid (*ca.* 2·5 g.) was crystallised from acetic acid, to give α-2 : 5-*dimethoxyphenacyl-α-methylmalonic acid*, m. p. 164—165° (gas evolution) (Found : C, 57·0; H, 5·6; OMe, 21·1. $C_{14}H_{16}O_7$ requires C, 56·8; H, 5·4; OMe, 20·9%). When this acid (1·0 g.) was heated at 205—210° for 30 min., then extracted with sodium carbonate solution (charcoal), and reprecipitated, it gave β-2 : 5-*dimethoxybenzoyl-α-methylpropionic acid* (*ca.* 0·5 g.), m. p. 116·5—118° (from benzene) (Found : C, 61·8; H, 6·2; OMe, 25·9. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·3; OMe, 24·6%).

(ii) The product (*ca.* 8·5 g., 66%), m. p. 102—112°, from methylsuccinic anhydride (6·0 g.),

[2] Fieser and Newman, *J. Amer. Chem. Soc.*, 1936, **58**, 2376; Newman and Orchin, *ibid.*, 1938, **60**, 586; Newman, *ibid.*, p. 1368; Newman and Orchin, *ibid.*, 1939, **61**, 244; Newman and Wise, *ibid.*, 1941, **63**, 2109.

[3] (*a*) Weizmann, Blum-Bergmann, and Bergmann, *J.*, 1935, 1370; (*b*) Newman, *J. Amer. Chem. Soc.*, 1937, **59**, 1003; Newman and McCleary, *ibid.*, 1941, **63**, 1542; Newman and Muth, *ibid.*, 1950, **72**, 5191.

[4] Geissman and Morris, *ibid.*, 1941, **63**, 1111.

[5] Cf. Newman and Lord, *ibid.*, 1944, **66**, 733.

[6] Bost and Howe, *ibid.*, 1951, **73**, 5864.

[7] Mayer and Stamm, *Ber.*, 1923, **56**, 1424.

p-dimethoxybenzene (6·9 g.), and aluminium chloride (13·5 g., 2 mols.) in nitrobenzene (50 ml.), after being kept at room temperature overnight,[8,9] was repeatedly crystallised from benzene, to give β-2 : 5-dimethoxybenzoyl-α-methylpropionic acid, m. p. 116·5—118° alone or mixed with a specimen prepared by the above method. The *methyl ester*, prepared by methanol and hydrogen chloride and crystallised from light petroleum (b. p. 40—60°), had m. p. 70—71° (Found : C, 63·3; H, 7·1; OMe, 33·3. $C_{14}H_{18}O_5$ requires C, 63·2; H, 6·8; OMe, 34·9%). Evaporation of the benzene mother-liquor from the first crystallisation left an oil (*ca.* 1·6 g.), which was probably the β-methyl-acid. With *s*-tetrachloroethane as a medium, the product (1·8 g., 14%) was a mixture of the α-methyl-acid (*ca.* 1·3 g.) and its β-methyl isomer (0·3 g.).

2-Methoxyacetophenone.—A mixture of 2-hydroxyacetophenone (10 g.), dimethyl sulphate (16 ml.), anhydrous potassium carbonate (37 g.), and dry acetone (100 ml.) was refluxed for 12 hr., then worked up as usual. 2-Methoxyacetophenone was obtained as a pale yellow oil, b. p. 245—246°/760 mm. Tahara [10] gives b. p. 240°/712 mm.

ω-Bromo-2-methoxyacetophenone.—This was prepared by a method similar to that reported for ω-bromo-2 : 5-dimethoxyacetophenone. The unstable oily product was immediately used without purification in the following experiment.

β-*o-Methoxybenzoyl-α-methylpropionic Acid.*—To a suspension of diethyl sodiomethylmalonate [from finely powdered sodium (0·6 g.) and methylmalonate (4·7 g.) in ether (10 ml.)], crude ω-bromo-*o*-methoxyacetophenone (6 g.) was gradually added with occasional shaking, and the mixture left for 1—2 hr., then worked up as usual. The product was repeatedly extracted with boiling light petroleum (b. p. 40—60°), and the combined extracts were concentrated. The ester which crystallised was repeatedly crystallised from benzene–light petroleum (b. p. 40—60°), to give *diethyl α-o-methoxyphenacyl-α-methylmalonate*, m. p. 89—90° (Found : C, 63·7; H, 6·8. $C_{17}H_{22}O_6$ requires C, 63·4; H, 6·8%).

Hydrolysis of this ester with 5% alcoholic potassium hydroxide solution (1·5 hours' refluxing) gave an acid, which was heated with dilute hydrochloric acid on a boiling-water bath till bubbling ceased (several hr.). The product was then dissolved in ether and extracted with sodium carbonate solution (charcoal). The semi-solid acid (*ca.* 1·3—1·5 g.) precipitated on acidification was methylated with dimethyl sulphate, potassium carbonate, and acetone. The ester was distilled in a vacuum (b. p. 186—190°/12 mm.), then hydrolysed with 5% alcoholic potassium hydroxide. The acid, crystallised from benzene–light petroleum (b. p. 40—60°), gave β-*o-methoxybenzoyl-α-methylpropionic acid*, m. p. 96—97° (Found : C, 65·2; H, 6·2; OMe, 13·8. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3; OMe, 14·0%).

Methylation with dimethyl sulphate was essential, since the product was a mixture of β-*o*-methoxy- and β-*o*-hydroxy-benzoyl-α-methylpropionic acid, the latter being predominant. The *hydroxy-acid* was obtained (m. p. 158·5—159·5°) by fractional crystallisation of the mixture from benzene (Found : C, 63·8; H, 5·8. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%). It gave a red colour with ferric chloride. The formation of this acid may be due to partial demethylation during heating with hydrochloric acid.

Action of 2 : 5-Dimethoxyphenylmagnesium Iodide on Succinic Anhydride, β-2 : 5-Dimethoxybenzoylpropionic Acid, and its Methyl Ester.—(i) An ethereal solution of 2 : 5-dimethoxyphenylmagnesium iodide [from 2-iodo-1 : 4-dimethoxybenzene [11] (26·4 g.) and magnesium (2·6 g.) in ether (40 ml.)] was added dropwise during 20 min. to a boiling benzene solution (100 ml.) of succinic anhydride (5 g.), and the experiment was carried out in a manner similar to that adopted in Part IV. The solid (A), insoluble in sodium carbonate, was filtered off and dried (*ca.* 4·5 g.). Repeated crystallisation from ethanol gave *γγ-di-2 : 5-dimethoxyphenylbutyrolactone*, m. p. 139—140° (Found : C, 67·0; H, 6·15; OMe, 33·9. $C_{20}H_{22}O_6$ requires C, 67·0; H, 6·15; OMe, 34·6%).

The cold sodium carbonate solution gave on acidification an oily acid (B) (*ca.* 3·0 g.), which was methylated with methyl iodide and potassium carbonate in acetone (12 hours' refluxing). The ester was hydrolysed with 5% alcoholic potassium hydroxide, and the acid was crystallised from benzene, to give β-2 : 5-dimethoxybenzoylpropionic acid, m. p. 106—107°, undepressed on admixture with an authentic specimen.[12]

The oil (C) left on evaporation of the ether–benzene mixture was dissolved in hot alcohol,

[8] Baddar, Fahim, and Fleifel, *J.*, 1955, 3302.
[9] Baddar, Fahim, and Fleifel, *J.*, 1955, 2199.
[10] Tahara, *Ber.*, 1892, **25**, 1308.
[11] Kauffmann and Fritz, *Ber.*, 1908, **41**, 4415.
[12] Dalal and Nargund, *J. Indian Chem. Soc.*, 1937, **14**, 406.

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and the solvent left to evaporate slowly. The precipitated product (D) (*ca.* 0·2 g.) was refluxed with glacial acetic acid (1·5 hr.), then repeatedly crystallised from the same solvent to give 2 : 2 : 5 : 5-*tetra*-(2 : 5-*dimethoxyphenyl*)*tetrahydrofuran*, m. p. 202—203° (Found: C, 70·3; H, 6·5; OMe, 37·1. $C_{36}H_{40}O_9$ requires C, 70·1; H, 6·5; OMe, 40·2%).

(ii) The experiment was repeated with β-2 : 5-dimethoxybenzoylpropionic acid (12 g.) to give a lactone (A) (1·7 g.), unchanged γ-keto-acid (6·7 g.), and a tetrahydrofuran (D) (0·7 g.).

(iii) The reaction between 2 : 5-dimethoxyphenylmagnesium iodide (2 mols.) and methyl β-2 : 5-dimethoxybenzoylpropionate (5 g.; 1 mol.) was carried out as described in Part IV. The acid (3·0 g.) extracted with sodium hydroxide solution was crystallised from light petroleum (b. p. 40—60°), to give 3 : 3-*di*-(2 : 5-*dimethoxyphenyl*)*prop*-2-*ene*-1-*carboxylic acid*, m. p. 134—136° (Found: C, 66·9; H, 6·15; OMe, 32·5. $C_{20}H_{22}O_6$ requires C, 67·0; H, 6·15; OMe, 34·6%). It discharged the colour of alkaline potassium permanganate.

The viscous oil (C) was treated as usual, to give β-2 : 5-dimethoxybenzoylpropionic acid (*ca.* 0·4 g.), and a solid (D) (0·4 g.) which, crystallised from acetic acid, gave 2 : 2 : 5 : 5-tetra-(2 : 5-dimethoxyphenyl)tetrahydrofuran, m. p. and mixed m. p. 202—203°.

Isomerisation of γγ-Di-2 : 5-dimethoxyphenylbutyrolactone.—The lactone was refluxed for 3 hr. with concentrated hydrochloric acid, and worked up as described by Baddar and El-Assal.[1] Crystallisation of the product from benzene–light petroleum (b. p. 40—60°) gave 3 : 3-di-(2 : 5-dimethoxyphenyl)prop-2-ene-1-carboxylic acid, m. p. and mixed m. p. 135—136°.

Unless otherwise stated, the following Grignard reactions were carried out as described in the above experiment.

Action of 2-Methoxy-1-naphthylmagnesium Iodide on Succinic Anhydride.—(i) The Grignard reagent [from 1-iodo-2-methoxynaphthalene (25·6 g., 2 mols.) in ether (50 ml.) and benzene (50 ml.)] was refluxed for 5 hr. with a benzene solution (100 ml.) of succinic anhydride (4·5 g.; 1 mol.). The acid (*ca.* 0·5 g.) precipitated on decomposition of the mixture was filtered off and mixed with the same acid (B) (3 g.) obtained from the carbonate solution. On crystallisation from benzene, β-2-methoxy-1-naphthoylpropionic acid was obtained in colourless needles, m. p. 135—136°, undepressed on admixture with an authentic specimen.[13]

The lactone (A) (*ca.* 0·2 g.) was first crystallised from glacial acetic acid, then repeatedly from benzene, to give γγ-*di*-(2-*methoxy*-1-*naphthyl*)*butyrolactone*, m. p. 236—238° (Found: C, 78·6; H, 5·6; OMe, 16·1. $C_{26}H_{22}O_4$ requires C, 78·4; H, 5·6; OMe, 15·6%).

The neutral solid (C) (8·5 g.) was identified as nerolin.

(ii) When 1 mol. of the Grignard reagent was used (3 hours' refluxing) the only products were the γ-keto-acid (*ca.* 4·0 g.) and nerolin (2·6 g.).

Action of o-Methoxyphenylmagnesium Bromide on β-2-Methoxy-1-naphthoylpropionic Acid.—The product from the Grignard reagent [from *o*-bromo-anisole (7·3 g., 2 mols.)] and β-2-methoxy-1-naphthoylpropionic acid (5 g.) contained the unchanged acid (*ca.* 3·2 g.) and a neutral brown oil (C). The latter was digested with alcohol, and the insoluble product (D) (*ca.* 0·2 g.) was refluxed with glacial acetic acid, then crystallised from the same solvent, to give 4-(2-*methoxy*-1-*naphthyl*)-1 : 1 : 4-*tri*-*o*-*methoxyphenylbuta*-1 : 3-*diene*, m. p. 195—196° (Found: C, 82·5; H, 5·9; OMe, 22·2. $C_{36}H_{32}O_4$ requires C, 81·8; H, 6·1; OMe, 23·5%).

The alcoholic mother-liquor, when kept, deposited a colourless product (*ca.* 0·4 g.) which, crystallised from ethanol, then repeatedly from benzene–light petroleum (b. p. 40—60°), had m. p. 161—162° (Found: C, 76·0; H, 6·2; OMe, 19·3. $C_{29}H_{28}O_5$ requires C, 76·3; H, 6·1; OMe, 20·4%). Analysis and absorption spectrum gave some evidence that it might be γ-*hydroxy*-*o*-*methoxy*-γ-(2-*methoxy*-1-*naphthyl*)*phenylbutyrophenone*.

Action of o-Methoxyphenylmagnesium Bromide on β-2-Methoxy-5-phenylbenzoylpropionic Acid and its Methyl Ester.—(i) The alkaline extract of the product from the Grignard reagent [from *o*-bromoanisole (6·6 g., 2 mols.)] and the acid [14] (5 g., 1 mol.) contained the unchanged keto-acid (*ca.* 2·4 g.) and a lactone (*ca.* 0·4 g.). The latter compound was repeatedly crystallised from ethanol, to give γ-*o*-*methoxyphenyl*-γ-(4-*methoxy*-3-*diphenylyl*)*butyrolactone*, m. p. 162—163° (Found: C, 76·4; H, 5·8; OMe, 17·4. $C_{24}H_{22}O_4$ requires C, 77·0; H, 5·9; OMe, 16·0%). The neutral product (D) (*ca.* 0·3 g.) was refluxed with glacial acetic acid to give an inseparable mixture, m. p. 176—178° (cleared at 185°).

(ii) The reaction between *o*-methoxyphenylmagnesium bromide (7·6 g., 2 mols.) and the ester (6 g., 1 mol.) gave a semi-solid acid (*ca.* 2·6 g.), which was repeatedly crystallised from

[13] Short, Stromberg, and Wiles, *J.*, 1936, 319.
[14] Fieser and Bradsher, *J. Amer. Chem. Soc.*, 1936, **58**, 1738.

benzene–light petroleum (b. p. 40—60°) to give 3-(4-*methoxy*-3-*diphenylyl*)-3-o-*methoxyphenyl*-*prop*-2-*ene*-1-*carboxylic acid*, m. p. 140—142°, depressed to 122—125° on admixture with the above keto-acid (Found : C, 76·2; H, 5·6; OMe, 16·0. $C_{24}H_{22}O_4$ requires C, 77·0; H, 5·9; OMe, 16·0%). It discharged the colour of alkaline potassium permanganate.

The neutral oily product (C) was treated as usual to give the γ-keto-acid (0·2 g.) and an inseparable mixture (0·7 g.).

Action of o-*Methoxyphenylmagnesium Bromide on* β-2-*Methoxy*-5-p-*methoxyphenylbenzoylpropionic Acid.*—The acid product from the interaction between the Grignard reagent [from *o*-bromoanisole (5·4 g., 2 mols.)] and the keto-acid [9] (4·5 g., 1 mol.) contained the unchanged acid (3 g.) and a lactone (A) (*ca.* 0·3 g.). Crystallisation of the lactone from ethanol gave γ-(4 : 4′-*dimethoxy*-3-*diphenylyl*)-γ-o-*methoxyphenylbutyrolactone*, m. p. 170—171° (Found : C, 74·4; H, 6·0; OMe, 23·2. $C_{25}H_{24}O_5$ requires C, 74·2; H, 6·0; OMe, 23·1%).

The neutral semi-solid (D) (*ca.* 0·4 g.) was refluxed with glacial acetic acid, then repeatedly crystallised from the same solvent, to give 5-(4 : 4′-*dimethoxy*-3-*diphenylyl*)*tetrahydro*-2 : 2 : 5-*tri*-o-*methoxyphenylfuran*, m. p. 202—203° (Found : C, 77·1; H, 6·3; OMe, 24·4. $C_{39}H_{38}O_6$ requires C, 77·7; H, 6·3; OMe, 25·7%).

Action of o-*Methoxyphenylmagnesium Bromide on* β-2 : 5-*Dimethoxybenzoylpropionic Acid.*—The reaction between the Grignard reagent [from *o*-bromoanisole (7·9 g., 2 mols.)] and the keto-acid (5 g., 1 mol.) gave traces of a lactone, which could not be identified, and the unchanged keto-acid (*ca.* 2·6 g.). The neutral solid (D) (*ca.* 0·5 g.) was repeatedly crystallised from benzene, to give 4-(2 : 5-*dimethoxyphenyl*)-1 : 1 : 4-*tri*-o-*methoxyphenylbutane*-1 : 4-*diol*, m. p. 219—220° (Found : C, 72·9; H, 6·6; OMe, 25·6; active H, 0·36. $C_{33}H_{36}O_7$ requires C, 72·8; H, 6·6; OMe, 28·5; active H, 0·37%).

Refluxing this diol with glacial acetic acid gave an inseparable mixture.

Action of o-*Methoxyphenylmagnesium Bromide on* β-2-*Methoxy*-5-*methylbenzoylpropionic Acid and its Methyl Ester.*—(i) The Grignard reagent [from *o*-bromoanisole (8·5 g., 2 mols.)] with this acid (5 g., 1 mol.) gave recovered keto-acid (3·2 g.) and γ-(2-*methoxy*-5-*methylphenyl*)-γ-o-*methoxyphenylbutyrolactone*, m. p. 149—150° (from ethanol) (Found : C, 72·7; H, 6·6; OMe, 19·9. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4; OMe, 17·1%). The neutral solid (D) (*ca.* 0·4 g.) was fractionally crystallised from acetic acid, to give *tetrahydro*-5-(2-*methoxy*-5-*methylphenyl*)-2 : 2 : 5-*tri*-o-*methoxyphenylfuran*, m. p. 233—234° (Found : C, 77·5; H, 6·6; OMe, 21·6. $C_{33}H_{34}O_5$ requires C, 77·6; H, 6·7; OMe, 24·3%).

(ii) The reaction between the above Grignard reagent (1 mol.) and the ester (6 g., 1 mol.) gave an acid (*ca.* 2·0 g.), which was repeatedly crystallised from benzene–light petroleum (b. p. 40—60°) to give 3-(2-*methoxy*-5-*methylphenyl*)-3-o-*methoxyphenylprop*-2-*ene*-1-*carboxylic acid*, m. p. 114·5—115·5° (Found : C, 73·6; H, 6·6; OMe, 18·0. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4; OMe, 17·1%). It decolorised alkaline potassium permanganate.

The neutral oil (C) gave the γ-keto-acid (*ca.* 2 g.) and tetrahydro-5-(2-methoxy-5-methylphenyl)-2 : 2 : 5-tri-*o*-methoxyphenylfuran (*ca.* 0·2 g.), m. p. and mixed m. p. 234—235°.

When 2 mols. of the Grignard reagent were used, no propene acid was isolated. The solid (*ca.* 1·9 g.), m. p. 210—220°, precipitated on decomposition of the Grignard complex, was crystallised successively from acetic acid, acetone, and acetic acid, to give 4-(2-*methoxy*-5-*methylphenyl*)-1 : 1 : 4-*tri*-o-*methoxyphenylbuta*-1 : 3-*diene*, m. p. 176—177°, depressed to 170° on admixture with the corresponding tetrahydrofuran (Found : C, 79·8; H, 6·7; OMe, 23·9. $C_{33}H_{32}O_4$ requires C, 80·5; H, 6·5; OMe, 25·2%).

From the neutral oil (C), tetrahydro-5-(2-methoxy-5-methylphenyl)-2 : 2 : 5-tri-*o*-methoxyphenylfuran (*ca.* 0·1 g.), m. p. and mixed m. p. 233—234°, was isolated.

Action of o-*Methoxyphenylmagnesium Bromide on* β-5-*Chloro*-2-*methoxybenzoylpropionic Acid and its Methyl Ester.*—(i) *o*-Methoxyphenylmagnesium bromide [from *o*-bromoanisole (8 g., 2 mols.)] reacted with the keto-acid (5 g., 1 mol.), to give γ-(5-*chloro*-2-*methoxyphenyl*)-γ-o-*methoxyphenylbutyrolactone* (0·4 g., crude), m. p. 153—154° (from ethanol) (Found : C, 64·8; H, 4·9; Cl, 10·2; OMe, 19·0. $C_{18}H_{17}O_4Cl$ requires C, 65·0; H, 5·1; Cl, 10·6; OMe, 18·9%), and 5-(5-*chloro*-2-*methoxyphenyl*)*tetrahydro*-2 : 2 : 5-*tri*-o-*methoxyphenylfuran* (0·6 g.; crude), m. p. 250—251° (from acetic acid) (Found : C, 72·4; H, 5·8; Cl, 6·3; OMe, 19·6. $C_{32}H_{31}O_5Cl$ requires C, 72·4; H, 5·8; Cl, 6·7; OMe, 23·4%). The product contained unchanged keto-acid (*ca.* 3·2 g.).

(i) The Grignard reagent [from *o*-bromoanisole (9 g., 2 mols)] reacted with the ester (6 g., 1 mol.) as usual, and the solid (1·2 g.) precipitated on decomposition was found to be the above

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tetrahydrofuran, m. p. and mixed m. p. 250—251°. The semi-solid acid (*ca.* 2 g.) was digested with light petroleum (b. p. 40—60°), then fractionally crystallised from benzene–light petroleum (b. p. 40—60°), to give two types of crystal which were mechanically separated. The predominant fraction, m. p. 120—122° (cleared at 136°), was repeatedly crystallised from the same solvent to give 3-(*5-chloro-2-methoxyphenyl*)-3-o-*methoxyphenylprop-2-ene*-1-*carboxylic acid*, m. p. 142—143° (shrinking at 140°) (Found: C, 64·9; H, 5·2; Cl, 10·4; OMe, 19·4. $C_{18}H_{17}O_4Cl$ requires C, 65·0; H, 5·1; Cl, 10·6; OMe, 18·9%). It decolorised alkaline potassium permanganate.

The neutral product (D) was triturated with benzene, then crystallised from glacial acetic acid to give another crop of the tetrahydrofuran. The benzene was evaporated, and the remaining viscous oil was dissolved in ethanol, and left to evaporate slowly. The precipitated product (*ca.* 0·4 g.) was crystallised from benzene–light petroleum (b. p. 50—60°), and the predominant crystals were mechanically separated (*ca.* 0·1 g.), then recrystallised from the same solvent to give colourless crystals, m. p. 125—126°, probably γ-(*5-chloro-2-methoxyphenyl*)-γ-*hydroxy*-o-*methoxy*-γ-o-*methoxyphenylbutyrophenone* (Found: C, 68·5; H, 5·9; Cl, 7·6; OMe, 20·6. $C_{25}H_{25}O_5Cl$ requires C, 68·1; H, 5·7; Cl, 8·1; OMe, 21·1%). This structure was supported by absorption spectra, but its full establishment was left for further investigation.

Action of Phenylmagnesium Iodide on Methylsuccinic Anhydride.—(i) Phenylmagnesium iodide [from iodobenzene (26·8 g., 2 mols.)] was added to methylsuccinic anhydride (7·5 g., 1 mol.), and worked up. The acid precipitated on acidification of the carbonate solution was crystallised from acetic acid, to give β-benzoyl-α-methylpropionic acid (1·0 g.), m. p. 140°, undepressed on admixture with an authentic specimen.[7] The aqueous mother-liquor gave, on concentration, a viscous oil, which was crystallised from light petroleum (b. p. 40—60°) to give the β-methyl-isomer (*ca.* 0·2 g.), m. p. and mixed m. p. 56—58°.[7] The mixture of lactones (A) (2·8 g.) was repeatedly crystallised from methyl alcohol to give α-methyl-γγ-diphenylbutyrolactone, m. p. and mixed m. p. 117—118°. The neutral oil (C) contained diphenyl. Isomerisation of the above lactone with concentrated hydrochloric acid was attempted unsuccessfully (5 hours' refluxing).

Action of Phenylmagnesium Iodide on β-*Benzoyl-α-methylpropionic acid and its Methyl Ester.*—(i) Phenylmagnesium iodide [from iodobenzene (12·6 g., 2 mols.)] reacted with the keto-acid (6 g., 1 mol.) to give a lactone (*ca.* 0·8 g.) and unchanged keto-acid (*ca.* 2·0 g.). Crystallisation of the lactone from methanol gave *α-methyl-γγ-diphenylbutyrolactone*, m. p. 117—118° (Found: C, 81·2; H, 6·2. $C_{17}H_{16}O_2$ requires C, 80·95; H, 6·3%).

The neutral product (D) was freed from iodobenzene and diphenyl by heating in a vacuum (b. p. 110—120°/4 mm.). The residue was crystallised from methanol to give the lactone.

(ii) Reaction between the Grignard reagent [from iodobenzene (14·2 g., 2 mols.)] and methyl β-benzoyl-α-methylpropionate (7 g., 1 mol.) gave an acid (*ca.* 3 g.), which was repeatedly crystallised from light petroleum (b. p. 40—60°), to give 1-*methyl*-3 : 3-*diphenylprop-2-ene*-1-*carboxylic acid*, m. p. 103—104° (*ca.* 0·6 g.) (Found: C, 81·3; H, 6·5. $C_{17}H_{16}O_2$ requires C, 80·95; H, 6·3%). It decolorised alkaline potassium permanganate. The neutral material (D) failed to give a pure product.

Action of p-*Tolylmagnesium Iodide on Methylsuccinic Anhydride.*—*p*-Tolylmagnesium iodide [from *p*-iodotoluene (28·6 g., 2 mols.)] with methylsuccinic anhydride (7·5 g., 1 mol.) gave a lactone and a mixture of keto-acids. The lactone was distilled at 255—265°/2 mm. (*ca.* 1 g.), then repeatedly crystallised from benzene–light petroleum (b. p. 40—60°) to give α-methyl-γγ-di-*p*-tolylbutyrolactone, m. p. and mixed m. p. 125—126°. The mixed acids were extracted with cold benzene, and the insoluble fraction was crystallised from glacial acetic acid to give α-methyl-β-*p*-toluoylpropionic acid, m. p. and mixed m. p. 169—170°[7] (*ca.* 1·3 g.). Evaporation of the benzene extract left an oil, which was distilled at 180—190°/2 mm. (*ca.* 1·2 g.) and crystallised from benzene–light petroleum (b. p. 40—60°) to give the β-methyl isomer (*ca.* 0·5 g.), m. p. and mixed m. p. 62—64°.[7] The neutral semi-solid (C) gave di-*p*-tolyl[15] (from acetic acid), m. p. and mixed m. p. 119—120°.

Action of p-*Tolylmagnesium Iodide on α-Methyl- and* β-*Methyl*-β-p-*toluoylpropionic Acid.*—(i) The Grignard reagent [from *p*-iodotoluene (21·2 g., 2 mols.)] with α-methyl-β-*p*-toluoylpropionic acid (10 g., 1 mol.) gave the unchanged keto-acid (*ca.* 5·5 g.) and a lactone (A) (*ca.* 1·2 g.). The latter, crystallised from benzene–light petroleum, gave *α-methyl-γγ-di*-p-*tolylbutyrolactone*, m. p. 125—126° (Found: C, 81·8; H, 7·4. $C_{19}H_{20}O_2$ requires C, 81·4; H, 7·1%). The neutral product (D) contained di-*p*-tolyl.

[15] Ullmann and Meyer, *Annalen*, 1904, **332**, 44.

(ii) The experiment was repeated with the β-methyl-keto-acid, to give the corresponding lactone (*ca.* 1·6 g.), b. p. 215—225°/3 mm.

Action of o-*Methoxyphenylmagnesium Bromide on Methylsuccinic Anhydride.*—(i) The Grignard reagent [from *o*-bromoanisole (24·6 g., 2 mols.)] with methylsuccinic anhydride (7·5 g., 1 mol.) gave a mixture of lactones (*ca.* 2·2 g.) and of keto-acids (*ca.* 1·7 g.). Trituration of the lactones with cold ethanol left an insoluble fraction (*ca.* 1·1 g.), which on repeated crystallisation from the same solvent gave γγ-di-*o*-methoxyphenyl-α-methylbutyrolactone, m. p. and mixed m. p. 126·5—127·5°. The crystals (*ca.* 0·3 g.), precipitated on slow evaporation of the alcohol used in trituration, were repeatedly crystallised from methanol, to give *γγ-di-o-methoxyphenyl-β-methylbutyrolactone*, m. p. 128—129°, depressed to 100° on admixture with a specimen of the above α-methyl isomer (Found: C, 73·3; H, 6·4; OMe, 20·8. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4; OMe, 19·9%).

The mixture of keto-acids was fractionally crystallised from benzene–light petroleum to give β-*o*-methoxybenzoyl-α-methylpropionic acid, m. p. 96—97°, undepressed on admixture with an authentic specimen (p. 1693). Concentration of the mother-liquor followed by dilution with light petroleum and repeated crystallisation of the precipitated product from light petroleum (b. p. 40—60°) gave *β-o-methoxybenzoyl-β-methylpropionic acid*, m. p. 55—57° (clear at 58°), depressed to 47° on admixture with the α-methyl acid (Found: C, 64·9; H, 6·4; OMe, 13·4. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3; OMe, 14·0%).

The neutral product (D) was refluxed with glacial acetic acid, filtered off (*ca.* 2 g.), then crystallised from benzene to give *tetrahydro-2 : 2 : 5 : 5-tetra-o-methoxyphenyl-3-methylfuran*, m. p. 222—223° (Found: C, 77·4; H, 6·6; OMe, 23·9. $C_{33}H_{34}O_5$ requires C, 77·6; H, 6·7; OMe, 24·3%).

(ii) When the experiment was repeated with 1 mol. of the Grignard reagent, the neutral product (*ca.* 1·0 g.) was an oil.

Action of o-*Methoxyphenylmagnesium Bromide on* β-o-*Methoxybenzoyl-α-methylpropionic Acid.*—*o*-Methoxyphenylmagnesium bromide [from *o*-bromoanisole (3·5 g., 2 mols.)] and β-*o*-methoxybenzoyl-α-methylpropionic acid (2 g., 1 mol.) gave recovered γ-keto-acid (*ca.* 0·6 g.) and a lactone (*ca.* 0·5 g.). The latter was repeatedly crystallised from ethanol, to give *γγ-di-o-methoxyphenyl-α-methylbutyrolactone*, m. p. 126·5—127·5° (Found: C, 72·8; H, 6·3; OMe, 22·0. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4; OMe, 19·9%). There was insufficient of the neutral solid (D), m. p. 200—208°, for identification.

Isomerisation of γγ-Di-o-methoxyphenyl-α-methylbutyrolactone.—Isomerisation of the lactone with concentrated hydrochloric acid as usual gave a product, m. p. 134—137°, which was repeatedly crystallised from benzene–light petroleum to give *3 : 3-di-o-methoxyphenyl-1-methylprop-2-ene-1-carboxylic acid*, m. p. 139—140° (Found: C, 73·4; H, 6·4; OMe, 21·05. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4; OMe, 19·9%). It decolorised alkaline potassium permanganate.

Action of p-*Methoxyphenylmagnesium Bromide on Methylsuccinic Anhydride.*—*p*-Methoxyphenylmagnesium bromide [from *p*-bromoanisole (24·6 g., 2 mols.)] with methylsuccinic anhydride (7·5 g., 1 mol.) gave a mixture of keto-acids, and an oily lactone (*ca.* 1·5 g.) which failed to solidify even after distillation at 250—260°/3 mm. (*ca.* 0·6 g.). The keto-acids (*ca.* 2·0 g.), repeatedly crystallised from acetic acid, gave β-*p*-methoxybenzoyl-α-methylpropionic acid (*ca.* 0·4 g.), m. p. 143—144°, undepressed on admixture with an authentic specimen.[16] Evaporation of the acetic acid mother-liquor left a viscous oil (*ca.* 1·3 g.) which gave a semicarbazone, m. p. 180°, undepressed on admixture with a specimen of the semicarbazone of the β-methyl acid, kindly provided by A. M. Fleifel.[8] The semi-solid (D) failed to solidify even after passing through an alumina column.

Action of p-*Methoxyphenylmagnesium Bromide on* β-p-*Methoxybenzoyl-α-methylpropionic Acid.*—*p*-Methoxyphenylmagnesium bromide [from *p*-bromoanisole (12·6 g., 2 mols.)] and β-*p*-methoxybenzoyl-α-methylpropionic acid (7·5 g., 1 mol.) gave a lactone (*ca.* 0·5 g.), which failed to solidify, and the unchanged keto-acid (*ca.* 3·5 g.). The neutral semi-solid (C) failed to give a crystalline product.

Action of α-Naphthylmagnesium Bromide on Methylsuccinic Anhydride.—α-Naphthylmagnesium bromide [from α-bromonaphthalene (27·4 g., 2 mols.)] was refluxed with methylsuccinic anhydride (7·5 g., 1 mol.) for 5 hr., and worked up. The alkaline extract gave a lactone (*ca.* 2·0 g.), and a semi-solid mixture of the keto-acids. The lactone was repeatedly crystallised from methanol, to give α-methyl-γγ-di-1-naphthylbutyrolactone, m. p. and mixed m. p.

[16] Mitter and De, *J. Indian Chem. Soc.*, 1939, **16**, 200.

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166—167°. The keto-acids were repeatedly crystallised from benzene, to give α-methyl-β-1-naphthoylpropionic acid [17] (*ca.* 1·5 g.), m. p. and mixed m. p. 122—123°. Evaporation of the benzene mother-liquor left a semi-solid (*ca.* 2·5 g.), which failed to solidify or give a crystalline semicarbazone. However, it gave 1-naphthoic acid on oxidation with potassium permanganate,[9] and so was probably β-methyl-β-1-naphthoylpropionic acid. The neutral product (D) contained naphthalene.

Action of α-Naphthylmagnesium Bromide on α-Methyl-β-1-naphthoylpropionic Acid.—The Grignard reagent [from α-bromonaphthalene (3·42 g., 2 mols.)] and the keto-acid (2 g., 1 mol.) gave unchanged keto-acid (*ca.* 1·2 g.), and a lactone (A) (*ca.* 0·1 g.), which was crystallised from methanol to give *α-methyl-γγ-di-1-naphthylbutyrolactone* in colourless crystals, m. p. 166—167° (Found: C, 84·5; H, 5·7. $C_{25}H_{20}O_2$ requires C, 85·2; H, 5·7%).

Action of 2 : 5-Dimethoxyphenylmagnesium Iodide on Methylsuccinic Anhydride.—The Grignard reagent [from 2-iodo-1 : 4-dimethoxybenzene [11] (23·0 g., 2 mols.)] and methylsuccinic anhydride (5 g., 1 mol.) gave mixtures of lactones (*ca.* 3·7 g.) and of keto-acids (2·8 g.). The lactones were crystallised from ethanol, to give γγ-di-(2 : 5-dimethoxyphenyl)-α-methylbutyrolactone, m. p. and mixed m. p. 149—150°. Concentration of the alcoholic mother-liquor precipitated two crops. The first crop, m. p. 120—128°, was rejected. The second crop, m. p. 115—117° (*ca.* 0·3 g.), was fractionally crystallised from methanol to give a crop, m. p. 120—125° (rejected), and a second crop (*ca.* 0·2 g.), m. p. 137—139°. This was repeatedly crystallised from the same solvent to give *γγ-di-(2 : 5-dimethoxyphenyl)-β-methylbutyrolactone*, m. p. 139—140°, depressed to 120—125° on admixture with the α-methyl isomer (Found: C, 67·4; H, 6·3. $C_{21}H_{24}O_6$ requires C, 67·7; H, 6·5%).

The mixture of keto-acids was proved by ferric chloride test to contain a demethylated product, so it was methylated with methyl iodide, potassium carbonate, and acetone. Hydrolysis of the ester (5% alcoholic potassium hydroxide) gave a semi-solid which, crystallised from benzene, gave β-2 : 5-dimethoxybenzoyl-α-methylpropionic acid (*ca.* 0·3 g.), m. p. and mixed m. p. 116·5—118°. Evaporation of the benzene mother-liquor gave an oily acid, probably a mixture of the α- and β-methyl-keto-acids, which failed to solidify or to give a solid semicarbazone.

The neutral solid (D) was refluxed with glacial acetic acid, which was then removed in a vacuum. The residue was crystallised from ethanol, then from benzene–light petroleum to give *2 : 2 : 5 : 5-tetra-(2 : 5-dimethoxyphenyl)tetrahydro-3-methylfuran*, m. p. 153·5—154·5° (Found: C, 70·3; H, 6·5; OMe, 40·4. $C_{37}H_{42}O_9$ requires C, 70·4; H, 6·7; OMe, 39·4%). The alcohol used in trituration of the neutral product (C) slowly afforded a product (*ca.* 0·2 g.), which was repeatedly recrystallised from benzene–light petroleum to give colourless crystals, m. p. 152—153·5°, depressed to 130—140° when mixed with the above tetrahydrofuran. It was probably *γγ-di-(2 : 5-dimethoxyphenyl)-γ-hydroxy-2 : 5-dimethoxy-α-methylbutyrophenone* (Found: C, 68·8; H, 6·6; OMe, 34·05. $C_{29}H_{34}O_8$ requires C, 68·2; H, 6·7; OMe, 36·5%). Although its structure was supported by absorption spectrum, its complete elucidation was left for further investigation.

Action of 2 : 5-Dimethoxyphenylmagnesium Iodide on β-2 : 5-Dimethoxybenzoyl-α-methylpropionic Acid and its Methyl Ester.—(i) The Grignard reagent [from 2-iodo-1 : 4-dimethoxybenzene (10·5 g., 2 mols.)] and the keto-acid (5 g., 1 mol.) gave recovered keto-acid (*ca.* 3·3 g.) and a lactone (*ca.* 0·8 g.), m. p. 120—125°. Repeated crystallisation of the lactone from ethanol gave *γγ-di-(2 : 5-dimethoxyphenyl)-α-methylbutyrolactone*, m. p. 149—150° (Found: C, 67·8; H, 6·5; OMe, 33·1. $C_{21}H_{24}O_6$ requires C, 67·7; H, 6·5; OMe, 33·3%). The neutral product (D) contained *p*-dimethoxybenzene.

(ii) The Grignard reagent [from 2-iodo-1 : 4-dimethoxybenzene (10 g., 2 mols.)] and methyl β-2 : 5-dimethoxybenzoyl-α-methylpropionate (5 g., 1 mol.) gave an acid (*ca.* 3·5 g.), which was repeatedly crystallised from benzene–light petroleum to give *3 : 3-di-(2 : 5-dimethoxyphenyl)-1-methylprop-2-ene-1-carboxylic acid* (0·4 g.), m. p. 152—153° (Found: C, 67·3; H, 6·5; OMe, 33·0. $C_{21}H_{24}O_6$ requires C, 67·7; H, 6·5; OMe, 33·3%). The neutral product (D) (*ca.* 0·6 g.) was filtered off from an oily fraction, and refluxed with glacial acetic acid, which was then removed under reduced pressure. The residue was crystallised from benzene–light petroleum to give 2 : 2 : 5 : 5-tetra-(2 : 5-dimethoxyphenyl)tetrahydro-3-methylfuran, m. p. and mixed m. p. 153·5—154·5°.

Isomerisation of γγ-Di-(2 : 5-dimethoxyphenyl)-α-methylbutyrolactone.—The lactone was

[17] Haworth, *J.*, 1932, 1125.

isomerised by concentrated hydrochloric acid. Crystallisation of the product from benzene–light petroleum gave 3 : 3-di-(2 : 5-dimethoxyphenyl)-1-methylprop-2-ene-1-carboxylic acid, m. p. and mixed m. p. 153—154°.

FACULTY OF SCIENCE, CAIRO UNIVERSITY,
CAIRO, EGYPT.

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322. β-*Aroylpropionic Acids. Part VIII.* The Effect of Substituents on the Absorption Spectra of Tetra-arylbutadienes. Tetra-aryltetrahydrofurans, 3 : 3-Diarylprop-2-ene-1-carboxylic Acids, and γγ-Diarylbutyrolactones.*

By F. G. BADDAR, (MRS.) ADIBA HABASHI, and Z. SAWIRES.

The structures of some more 2 : 2 : 5 : 5-tetra-aryltetrahydrofurans and 1 : 1 : 4 : 4-tetra-arylbuta-1 : 3-dienes are confirmed by comparing their absorption spectra with those of the most similar γγ-diarylbutyrolactones and 3 : 3-diarylprop-2-ene-1-carboxylic acids, respectively, and with those of the tetra-aryltetrahydrofurans and tetra-arylbutadienes studied by Baddar and Sawires.[1]

The effect of substituents on the absorption spectra of these compounds is also investigated.

THE structures of the tetra-aryltetrahydrofurans and the tetra-arylbuta-1 : 3-dienes which were obtained by the action of arylmagnesium halides on succinic anhydride, methylsuccinic anhydride, and β-aroyl- and β-aroyl-α-methyl-propionic acids and their esters,[2] have been established by comparing their absorption spectra with those of the compounds studied previously,[1] and with those of the corresponding lactones and carboxylic acids, respectively. The study revealed also the effect of substituents and their position on these spectra.

The spectra were measured with a Beckman DU Quartz spectrophotometer, the tetra-aryltetrahydrofurans and the tetra-arylbutadienes being dissolved in " AnalaR " acetic acid–95% alcohol (1 : 3 v/v), the lactones and unsaturated carboxylic acids in 95% ethyl alcohol. The results are summarised in the Table.

Lactones and Tetrahydrofurans.—The absorption spectra of the lactones were similar in their general features to those studied by Baddar and Sawires.[1] Thus, the absorption of γγ-diphenyl- (I*a*) and γγ-di-*o*-methoxyphenyl-α-methylbutyrolactone (I*b*) were identical with those of γγ-diphenyl- and γγ-di-*o*-methoxyphenyl-butyrolactone, respectively.[1]

The close relationship between the absorption curves for γ-(2-methoxy-5-methylphenyl)-γ-*o*-methoxyphenyl- (I*c*) and γ-(5-chloro-2-methoxyphenyl)-γ-*o*-methoxyphenyl-butyrolactone (I*d*) on one hand, and that of (I*b*) on the other, gives evidence for their similarity in structure.

The curves for γγ-di-2 : 5-dimethoxyphenyl- (I*e*) and γγ-di-2 : 5-dimethoxyphenyl-α-methyl-butyrolactone (I*f*) are identical. They agree with the absorption of quinol ($\lambda_{max.}$ 294 mμ; ε 3100)[3] with nearly twice the intensity. The bathochromic shift and the large increase in intensity of absorption of these compounds, compared with results for γγ-di-*o*-methoxyphenylbutyrolactone[1] and compound (I*b*), respectively, are associated with the introduction of the second methoxyl group (cf. phenol[3] and quinol). The replacement of the *o*-methoxyphenyl group by the 4-methoxy-3-diphenylyl and 4 : 4′-dimethoxy-3-diphenylyl group (I*g* and *h*, respectively) causes a ten-fold increase in intensity of absorption.

* Part VII, preceding paper.

[1] Baddar and Sawires, *J.*, 1955, 4469.
[2] Baddar, El-Assal, and Habashi, preceding paper.
[3] Morton and Stubbs, *J.*, 1940, 1347; Morton and Sawires, *ibid.*, p. 1052.

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No.	R	Ar	Ar′	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	$\lambda_{min.}$ mμ)	$\varepsilon_{min.}$
(I)	*Lactones* Ar′ArC(O)·CH_2·CHR·CO						
a	Me	Ph	Ph	248 i	347	243·5	288
				255 i	436		
				258·5	521		
				263 i	419		
b	Me	*o*-MeO·C_6H_4	*o*-MeO·C_6H_4	272	4740	242	278
				278	4620	275·5	4560
c	H	2-MeO-5-Me·C_6H_3	*o*-MeO·C_6H_4	278	4820	244	327
d	H	2-MeO-5-Cl·C_6H_3	*o*-MeO·C_6H_4	279	4630	248	441
e	H	2 : 5-$(MeO)_2C_6H_3$	2 : 5-$(MOe)_2C_6H_3$	294	7980	254	455
f	Me	2 : 5-$(MeO)_2C_6H_3$	2 : 5-$(MeO)_2C_6H_3$	294	7940	253	378
g	H	2-MeO-5-Ph·C_6H_3	*o*-MeO·C_6H_4	263·5	20,850	235	6680
h	H	2-MeO-5-(C_6H_4·OMe-*p*)·C_6H_3	*o*-MeO·C_6H_4	267·5	25,460	263·5	6100
(II)	*Tetrahydrofurans* Ar′ArC(O)·CH_2·CHR·CAr′$_2$						
a	Me	*o*-MeO·C_6H_4	*o*-MeO·C_6H_4	274	8240		
				277 i	7925		
b	H	2-MeO-5-Me·C_6H_3	*o*-MeO·C_6H_4	276 i	7970		
				278	8160		
c	H	2-MeO-5-Cl·C_6H_3	*o*-MeO·C_6H_4	274 i	7740		
				278·5	8040		
d	H	2 : 5-$(MeO)_2C_6H_3$	2 : 5-$(MeO)_2C_6H_3$	289 i	13,100		
				292	13,520		
e	Me	2 : 5-$(MeO)_2C_6H_3$	2 : 5-$(MeO)_2C_6H_3$	289 i	13,370		
				292	13,900		
f	H	2-MeO-5-(C_6H_4·OMe-*p*)·C_6H_3	*o*-MeO·C_6H_4	269 i	27,650		
				271	27,860		
				272 i	27,650		
(III)	*Butadienes* Ar′ArC:CH·CH:CAr′$_2$						
a	—	2-MeO-5-Me·C_6H_3	*o*-MeO·C_6H_4	292·5 i	17,750	267·5	13,390
				337·5	25,800		
				339 i	25,750		
b	—	2-MeO·$C_{10}H_6$ (1)	*o*-MeO·C_6H_4	292·5 i	19,350	267	15,520
				336 i	26,670		
				339	26,740		
(IV)	*Acids* Ar′ArC:CH·CHR·CO_2H						
a	Me	*o*-MeO·C_6H_4	*o*-MeO·C_6H_4	281	6190	270	5500
b	H	2-MeO-5-Me·C_6H_3	*o*-MeO·C_6H_4	284	4950	271·5	4470
c	H	2-MeO-5-Cl·C_6H_3	*o*-MeO·C_6H_4	285·5	5970	271	4910
d	H	2 : 5-$(MeO)_2C_6H_3$	2 : 5-$(MeO)_2C_6H_3$	300	8000	273	2850
e	Me	2 : 5-$(MeO)_2C_6H_3$	2 : 5-$(MeO)_2C_6H_3$	299	8350	273	3390
f	H	2-MeO-5-Ph·C_6H_3	*o*-MeO·C_6H_4	248 i	25,980	230·5	22,020
				250 *	26,080	251	26,040
				252 *	26,080		
				255 i	25,940		
	(*o*-MeO·C_6H_4)$_2$CH·OH			273	4990	244	361
				277 i	4680		
	1-(2 : 5-Dimethoxyphenyl)-1 : 4 : 4-tri-*o*-methoxyphenylbutane-1 : 4-diol (VII*a*)			272 i	7430	247	831
				279	8210		
				290 i	3900		

i = Inflexion (approx.). * Poor persistence.

A similar relation stands for anisole ($\lambda_{max.}$ 265 mμ; ε 2300),[4] 4-methoxydiphenyl ($\lambda_{max.}$ 261 mμ; ε 21,000),[5] and 4 : 4′-dimethoxydiphenyl ($\lambda_{max.}$ 264 mμ; ε 24,610; in EtOH)[6] (Williamson and Rodebush[7] gave for the last compound $\lambda_{max.}$ 263 mμ; ε 21,700; in *n*-hexane).

The curves for the tetrahydrofuran derivatives (II*a*—*e*) are identical with those of the related lactones (I*b*—*f*, respectively) with nearly twice the absorption intensity.

[4] Wolf and Herold, *Z. phys. Chem.*, 1931, **12**, *B*, 201; Wolf and Strasser, *ibid.*, 1933, **21**, *B*, 389.
[5] Burawoy and Chamberlain, *J.*, 1952, 2310.
[6] Baddar and Sawires, unpublished work.
[7] Williamson and Rodebush, *J. Amer. Chem. Soc.*, 1941, **63**, 3018.

The absorption intensity of 5-(4 : 4′-dimethoxy-3-diphenylyl)tetrahydro-2 : 2 : 5-tri-*o*-methoxyphenylfuran (II*f*) is roughly equal to the sum of the intensities for γγ-di-*o*-methoxyphenylbutyrolactone [1] and 5-(4 : 4′-dimethoxy-3-diphenylyl)-γ-*o*-methoxyphenylbutyrolactone (I*h*).

The close relation between the absorption of the above-mentioned furans and the related lactones, as well as of the furans studied by Baddar and Sawires,[1] is strong evidence for the structure assigned to these compounds.

Dienes and Acids.—The curves for the tetra-arylbutadienes (III*a* and *b*) agree closely with those for 4-*o*-ethoxyphenyl-1 : 1 : 4-tri-*o*-methoxyphenyl- and 1 : 1 : 4-tri-*o*-ethoxyphenyl-4-*o*-methoxyphenyl-buta-1 : 3-diene.[1] This, as well as the fluorescence under ultraviolet irradiation (mercury-arc quartz lamp),[1] is strong evidence for the structure assigned to these compounds.

The intensity of absorption of 3 : 3-di-*o*-methoxyphenyl-1-methylprop-2-ene-1-carboxylic acid (IV*a*) is identical with that of 3 : 3-di-*o*-methoxyphenylprop-2-ene-1-carboxylic acid,[1] and much lower than those of 3 : 3-diphenyl- and 3 : 3-di-*p*-methoxyphenylprop-2-ene-1-carboxylic acid.[1] This is attributed to the steric inhibition of resonance of the *o*-methoxyphenyl group with the ethylenic linkage,[1] a phenomenon even more pronounced with the acids (IV*b*—*e*), in which the substituent in position 5′ exerts an additional steric effect. As a result the acids have spectra very close to those of the corresponding lactones (I*c*—*f*, respectively), with a slight bathochromic shift (*ca.* 6 mμ), indicating very strong inhibition of resonance between the disubstituted phenyl groups and the ethylenic linkage.

The butane-1 : 4-diol structure assigned to the compound (VII*a*) of the preceding paper was supported by its absorption spectrum, which is nearly equivalent to the summation of those for di-*o*-methoxyphenylmethanol and the mean values for γγ-di-*o*-methoxyphenylbutyrolactone and (I*e*).

FACULTY OF SCIENCE, CAIRO UNIVERSITY,
CAIRO, EGYPT.

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323. *Alkyl Sulphates. Part II.* Spectra of the* cyclo*Hexylammonium Salts in the* 800 *cm.*$^{-1}$ *Region.*

By R. A. G. CARRINGTON and H. C. EVANS.

For some 30 alkyl *cyclo*hexylammonium sulphates an absorption band of medium strength has a frequency of 790 cm.$^{-1}$ for all compounds having the substituent group attached at an even-numbered position on the hydrocarbon chain, whereas for odd-numbered substitution the frequency varies between 837 and 810 cm.$^{-1}$. Its position does not depend upon the number of carbon atoms in the hydrocarbon chain. Evidence is presented which suggests that the band arises from the skeletal stretching C–C modes in the hydrocarbon chain, but the possibility of the band's being assigned to another mode cannot be excluded.

IN Part I * we described the measurement of critical micelle concentrations as a means of identifying sodium alkyl sulphates $CHR^1R^2{\cdot}O{\cdot}SO_2{\cdot}ONa$, where R^1 and R^2 are unbranched. This property, together with molecular weight, affords satisfactory identification for pure compounds, but for mixtures the critical micelle concentration is of but limited value. Accordingly, the infrared spectra of the alkyl sulphates were examined to locate bands characteristic of the position of the substitutent group on the chain CHR^1R^2. An absorption band in the 800 cm.$^{-1}$ region was found to vary in a way which appears to be of theoretical interest.

* Part I, *J.*, 1956, 579.

La Lau and Dahmen [1] found that, whereas the sodium alkyl sulphates are insoluble in the organic solvents spectroscopically most suitable, the alkyl *cyclo*hexylammonium sulphates are soluble in carbon disulphide. *cyclo*Hexylammonium chloride, from which these salts are prepared, is readily available pure; as a paste with white oil its spectrum showed that under the conditions used there would be 90—95% transmission over the 1250—800 cm.$^{-1}$ range for the *cyclo*hexylammonium ion.

As in Part I, L denotes the number of carbon atoms in the hydrocarbon chain CHR^1R^2, and P the position of the sulphate group along that chain.

Results and Discussion

Spectra of Alkyl cyclo*Hexylammonium Sulphates.*—In preliminary work the infrared spectra of the *cyclo*hexylammonium tetradecyl sulphates ($L = 14$; $P = 1, 2, 3, 4, 5, 7$) in carbon disulphide and in the solid state were examined from 1450 to 650 cm.$^{-1}$. These spectra showed systematic differences in the 800 cm.$^{-1}$ region, and accordingly the remainder of the alkyl sulphates were examined particularly in this region. Fig. 1 shows the relevant portions of the spectra, except that of *cyclo*hexylammonium 1-tetradecylpentadecyl sulphate which has no specific absorption in this region.

Fig. 1. *Spectra near 800 cm.$^{-1}$ of alkyl* cyclo*hexylammonium sulphates.*

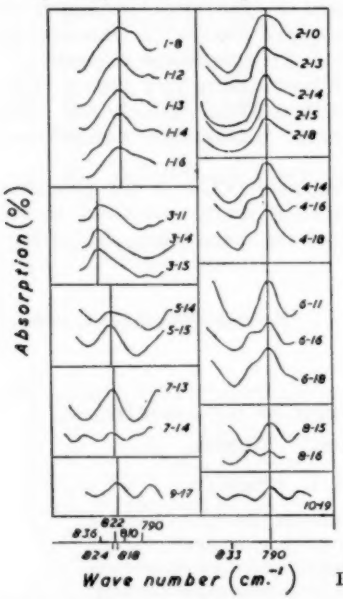
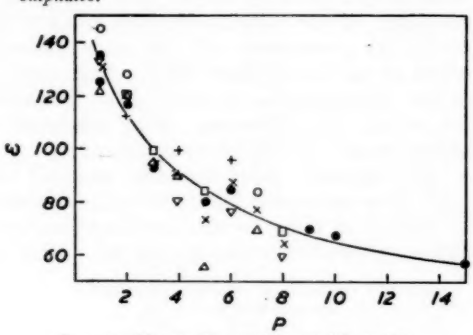


Fig. 2. *Decrease in* ε *with movement of substituent towards medial position in alkyl* cyclo*hexylammonium sulphates.*



L = ○ 13, △ 14, □ 15, ▽ 16, + 18, ● others, × average.

For identification of compounds, (P followed by L) see Table 3.

In the 800 cm.$^{-1}$ region each compound gives rise to an absorption band which has three salient features. First, its frequency depends on the position of the SO_4 group on the hydrocarbon chain; when P is even, the band occurs at 790 cm.$^{-1}$; when P is odd (1, 3, 5, 7, 9) it occupies the frequencies 810, 836, 824, 822, 818 respectively. Secondly, its position is independent of L, at any rate over the range $8 \leqslant L \leqslant 19$. Thirdly, when the molar extinction coefficient ε at the peak is plotted against P a smooth curve can be drawn (Fig. 2).

[1] La Lau and Dahmen, Paper presented at International Colloquium on Applied Spectroscopy, Amsterdam, May 1956.

Interpretation.—That the values of ε lie about a smooth curve appears to indicate that the band in all compounds is associated with a single mode of vibration. It is not attributable to S–O stretching,[2] although La Lau and Dahmen [1] discuss the possibility that a band near 810 cm.$^{-1}$ for the dodecyl and tetradecyl sulphates is due to a covalent S–O stretching. That ε becomes less as the SO_4 group is removed from the vicinity of a terminal carbon atom and is not markedly or systematically affected by changes in L indicate that the mode of vibration is influenced mostly by groupings in the shorter branch of the carbon chain. When the substituent group is sufficiently far removed from a terminal carbon atom, as in *cyclo*hexylammonium 1-tetradecylpentadecyl sulphate, no specific absorption is evident.

Spectra in the Solid State of Other Salts of $CHR^1R^2{\cdot}O{\cdot}SO_2{\cdot}OH$.—To investigate the spectra further the following compounds were examined: Tri-(2-hydroxyethyl)ammonium tetradecyl sulphate ($L = 14$, $P = 1$) and 1-propylundecyl sulphate ($L = 14$, $P = 4$); sodium, potassium, ammonium, and tri-(2-hydroxyethyl)ammonium salts of 1-methyltridecyl sulphate ($L = 14$, $P = 2$). The sodium, potassium, and ammonium salts showed in the 800 cm.$^{-1}$ region the major bands found in the spectrum of solid *cyclo*hexylammonium 1-methyltridecyl sulphate but not the band at 790 cm.$^{-1}$, which is also absent from the spectrum of *cyclo*hexylammonium chloride. Hence the band arises from interactions of vibrations of more than one part of the molecule. For each of the three isomers the spectrum of the tri-(2-hydroxyethyl)ammonium salt was essentially the same as that of the *cyclo*hexylammonium salt. One may therefore deduce that the band of medium strength near 800 cm.$^{-1}$ has arisen from the addition of a heavy substituent group to the paraffinic part of the molecule, and is associated with vibrations in the hydrocarbon chain. Brown, Sheppard, and Simpson [3] detected a band at 795 cm.$^{-1}$ in the spectrum of *n*-tetradecane and *n*-decane (but not in *n*-dodecane), strong in the crystalline and weaker in the liquid state.

Spectra of Similar Molecules in the Liquid State.—Sheppard and Simpson found a weak band at 840—810 cm.$^{-1}$ in the spectra of the *n*-paraffins; its frequency in paraffins of even carbon number is less than in those containing an odd number.[4] Kohlrausch [5] examined the Raman spectra of the *n*-paraffins from $L = 5$ to $L = 12$, and found prominent bands varying in the same way in the same frequency range. Sheppard and Simpson assign this band to the lower limiting skeletal stretching modes of non-planar isomers.[4] Williams and Moscher [6] found in the spectra of alkyl hydroperoxides (C_3—C_{10}) a band of alternating frequency in the 830 cm.$^{-1}$ region for α-substitution. A band in the 770 cm.$^{-1}$ region appears to alternate in frequency as the substituent is moved along the chain, but this effect could not be confirmed from the scanty data given. Kohlrausch [7] found the same alternating frequency near 800 cm.$^{-1}$ in the Raman spectra of *n*-paraffinic alcohols.

We have examined the infrared spectra of the isomeric tetradecanols with the hydroxyl group attached in the 1, 2, 3, 4, 5, and 7 positions. Near 800 cm.$^{-1}$ the only band is at 785 cm.$^{-1}$, weak in tetradecan-3-ol and of medium strength in tetradecan-5-ol. In general, information on the changes in frequency caused by movement of the substituent group along a hydrocarbon chain of fixed length or on the effect of substituents other than hydroxyl is small.

Assignment of Band in 800 cm.$^{-1}$ Region.—It is probable that this band can be assigned either to the CH_2 rocking modes or to the skeletal stretching C–C modes of non-planar isomers. In the absence of nearby bands of comparable intensity, we assume that the relevant band of each spectrum originates from the same single rocking or stretching mode. In an attempt to decide which mode of vibration is involved, the following evidence was

[2] Kohlrausch, "Raman Spectra," Leipzig, 1943, pp. 411—417.
[3] Brown, Sheppard, and Simpson, *Discuss. Faraday Soc.*, 1950, **9**, 261.
[4] Sheppard and Simpson, *Quart. Rev.*, 1953, **7**, 19.
[5] Kohlrausch and Köppl, *Z. phys. Chem.*, 1934, *B*, **26**, 209.
[6] Williams and Moscher, *Analyt. Chem.*, 1955, **27**, 517.
[7] Kohlrausch, ref. 2, p. 237.

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collected: (1) Tschamler [8] has observed that in hydrocarbons the CH_2 rocking frequencies move regularly to a limiting value as the chain length increases; in our spectra there is no progressive shift in frequency as the length of a hydrocarbon branch R^1 or R^2 is increased. (2) The band is not split in the spectra of the solid *cyclo*hexylammonium tetradecyl sulphates; this suggests that it does not arise from the CH_2 rocking mode. (3) The band intensity decreases as the molecule approaches symmetry (*i.e.*, as the sulphate group moves towards a medial position on the hydrocarbon chain). A CH_2 rocking mode can hardly be responsible for such a change. (4) In the spectra of unbranched-chain alcohols the skeletal modes are usually enhanced by the presence of the polar C–O bond [9] (although we have not been able to detect this effect in the 800 cm.$^{-1}$ region in the tetradecanols examined); since the C–O bond in alkyl sulphates is undoubtedly polar, it should have a similar effect. (5) If the $C_6H_{11}\cdot\overset{+}{N}H_3\cdot O\cdot SO_2\cdot O$-group is regarded as being responsible for differences between the spectra of the alkyl *cyclo*hexylammonium sulphates and those of the corresponding paraffins because of its inertia in altering the vibrations of the paraffinic part of the molecule, then its mass will affect the stretching modes of the hydrocarbon chain rather than the CH_2 rocking modes of the individual carbon atoms.

The balance of evidence favours a C–C skeletal vibration. Assuming that the band arises from vibrations in the shorter portion (R^1) of the hydrocarbon chain, we can attempt a more detailed analysis of the individual spectra. The alkyl sulphates can be divided into four groups according as the number of C–C bonds in the two branches of the hydrocarbon chain is odd or even and according as P is odd or even. In the following Table, frequencies in col. 7 are observed values of the major band. Those in col. 8 are

Group	P	L	Total no. of C–C bonds ($L-1$)	No. of C–C bonds in R^1 branch	No. of C–C bonds in R^2 branch	Frequency (cm.$^{-1}$) for R^1 branch	Frequency (cm.$^{-1}$) for R^2 branch
a	even	even	odd	odd	even	790	*ca.* 810
b	odd	,,	,,	even	odd	>790	790
c	even	odd	even	odd	,,	790	790
d	odd	,,	,,	even	even	>790	*ca.* 810

obtained by induction, and the plausibility of the assumptions made above rests on whether these bands can be detected in the spectra; the frequencies given will of course be those of minor bands, or, more probably, shoulders. In fact, the majority of Group *a* and *c* compounds conform to the predictions given in col. 8, whilst in Groups *b* and *d* only a small number of compounds have minor bands in the positions predicted. Also, the molar extinction coefficients at 790 cm.$^{-1}$ for Group *c* compounds should be greater than values for corresponding Group *a* compounds. Indeed, the molar extinction coefficients of compounds in which $P = 2$ are slightly greater for odd than for even values of L ("slightly" because the long-chain R^2 exerts only a very minor effect when $P = 2$); ε for *cyclo*hexylammonium 1-heptyloctyl sulphate ($L = 15$, $P = 8$) is considerably greater than the value for the 1-heptylnonyl sulphate ($L = 16$, $P = 8$), and ε for *cyclo*hexylammonium 1-pentylhexyl sulphate ($L = 11$, $P = 6$) is greater than the value for the 1-pentylundecyl sulphate ($L = 16$, $P = 6$) but less than for the 1-pentyltridecyl compound ($L = 18$, $P = 6$). Again, for symmetrical Group *d* compounds the molar extinction coefficients of the major band should be enhanced; thus *cyclo*hexylammonium 1-hexylheptyl sulphate ($L = 13$, $P = 7$) has $\varepsilon = 83{\cdot}8$ compared with $\varepsilon = 69{\cdot}7$ for *cyclo*hexylammonium 1-hexyloctyl sulphate ($L = 14$, $P = 7$). Overall, it appears that, although the balance of evidence is somewhat in favour of the assumptions made, some factor has been overlooked.

This hypothesis does not explain the position of the 810 cm.$^{-1}$ band in the spectra of the primary alkyl sulphates. If the major band in the 800 cm.$^{-1}$ region is assigned to C–C skeletal stretching vibrations in the shorter part of the hydrocarbon chain, it should

[8] Tschamler, *J. Chem. Phys.*, 1954, **20**, 1845.
[9] Brown, Sheppard, and Simpson, *Phil. Trans.*, 1954, **247**, 35.

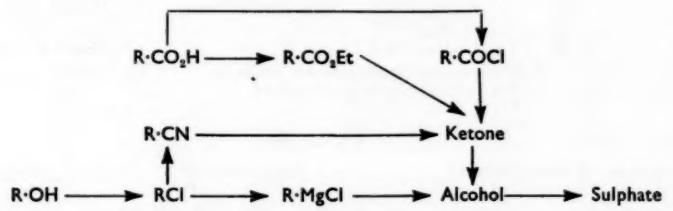
be absent from the spectra of the primary alkyl sulphates; and in fact there is no band at *ca.* 855 cm.$^{-1}$, the frequency at which one might be expected if the frequencies for the other odd values of P are extrapolated to $P = 1$ (Fig. 1). It is therefore possible that the 810 cm.$^{-1}$ band is not part of the P (odd) series as regards its position, although as regards its intensity the band is not anomalous because ε for the primary alkyl sulphates conforms with the other data (Fig. 2).

Calculations showed that the frequency could not be localised in either of the chains R^1 and R^2 and would appear to depend on the existence of a C–O bond. A model consisting of a normal carbon chain with a heavy substituent linked to it through an oxygen atom might well account for the effect, provided that the C–O vibration were only loosely coupled to the chain vibrations.

Experimental

Synthesis of Sodium Alkyl Sulphates.—For all except two compounds each of the steps is common to several preparations. The seven different steps are briefly described and are followed by Tables giving the nature and analytical details of the intermediate products. In the Tables each entry begins with the key number of the alkyl sulphate being made (see Table 3). In several instances one of the intermediate compounds was made by more than one route, and the entry appears twice in the Tables.

The starting point for each synthesis is the alkanol R·OH or the acid R·CO_2H; from these the chloride or the acid chloride was made by reaction with thionyl chloride. The various routes are summarised by the following scheme:



It was necessary to make, by standard methods, decanol (n_D^{20} 1·4372; b. p. 120°/12 mm.) from octanol, undecanol (n_D 1·400; b. p. 127°/14 mm.) from pelargonic acid, and pentadecanoic acid (m. p. 52·3°) from myristic acid.

1. *Preparation of Ketones.*—(a) *Claisen autocondensation.*[10] Standard methods were used except that sodium ethoxide was replaced by a suspension of sodium in toluene (see Table 1*a*).

(b) *Reaction between acid chloride and metal alkyl.* The acid chloride was added to the metal alkyl (*via* the Grignard reaction) in dry ether at such a rate that gentle refluxing was maintained, 4N-acid was added until the two phases were clear, and the aqueous layer was then separated and washed with ether. The combined ether layers were washed successively with N-acid, 10% sodium hydroxide solution, and water. The liquid was dried ($MgSO_4$) and distilled under reduced pressure, and the product was further purified by crystallisation from methanol (see Table 1*b*).

(c) *Reactions between alkyl cyanide and Grignard compound.* These are summarised in Table 1*c*.

(d) *Undecan-6-one and nonacosan-15-one.* Undecan-6-one was prepared from hexanoic acid by Herbst and Manske's method.[11] To prepare nonacosan-15-one, tetradecyl chloride was gradually added to lithium in dry ether in a nitrogen atmosphere and refluxed for 1 hr. The cooled, filtered product was poured on a large excess of solid carbon dioxide, dilute hydrochloric acid added, and the ether layer separated. After removal of the ether the *ketone* was crystallised from benzene–ethanol (yield 53%) (Found: C, 82·4; H, 13·9; CO, 6·6. $C_{29}H_{58}O$ requires C, 82·5; H, 13·7; CO, 6·6%).

2. *Preparation of Alcohols.*—(a) *Reduction of the ketone.* Reductions were effected chiefly

[10] Briese and McElvain, *J. Amer. Chem. Soc.*, 1933, **55**, 1699.
[11] Herbst and Manske, *Org. Synth.*, Coll. Vol. II, 1944, 389.

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by the Meerwein–Pondorff–Verley method (aluminium *iso*propoxide) and by hydrogen over Raney nickel. In the latter, a solution in alcohol was reduced with hydrogen at 135° and 70 atm. over Raney nickel for 17 hr. After separation of the catalyst the alcohol was distilled under reduced pressure and crystallised from light petroleum (see Table 2*a*).

(b) *Grignard compound + aldehyde.* See Table 2*b*.

(c) *Grignard compound + ethyl formate.* See Table 2*c*.

(d) *n*-Tetradecanol was made from dodecyl chloride *via* reaction with the sodium derivative of diethyl malonate; the resulting ester was hydrolysed to the free dibasic acid, which was decarboxylated by heating. The tetradecanoic acid thus obtained was reduced to tetradecanol by the Bouveault–Blanc reaction.

TABLE 1*a*.

Key no. of alkyl sulphate		Starting material		
P	*L*		B. p.	n_D^{20}
8	15	$C_7H_{15}\cdot CO_2C_2H_5$	94—98°/16 mm.	1·4180
9	17	$C_8H_{17}\cdot CO_2C_2H_5$	110—112°/20 mm.	—
10	19	$C_9H_{19}\cdot CO_2C_2H_5$	147—149°/44 mm.	1·4260

TABLE 1*b*.

Key no. of alkyl sulphate		Acid chloride		Grignard precursor	Metal alkyl
P	*L*		B. p.		
4	16	$C_3H_7\cdot COCl$	102—103°/765 mm.	$C_{12}H_{25}Cl$ *	$Cd(C_{12}H_{25})_2$
4	18	$C_{14}H_{29}\cdot COCl$	148—153°/3 mm.	C_2H_7Br †	$Cd(C_2H_7)_2$
5	14	$C_9H_{19}\cdot COCl$ ‡	104°/18 mm.	C_4H_9Br †	$Zn(C_4H_9)_2$
5	15	$C_{10}H_{21}\cdot COCl$	129—131°/17 mm.	C_4H_9Br †	$Cd(C_4H_9)_2$
5	19	$C_{14}H_{29}\cdot COCl$	—	"	"
6	16	$C_{10}H_{21}\cdot COCl$	—	$C_5H_{11}Br$ †	$Cd(C_5H_{11})_2$

* For physical properties see Table 2*b*. ‡ n_D^{20} 1·4399.
† Not prepared in this laboratory.

TABLE 1*c*.

Key no. of alkyl sulphate		Alkyl cyanide		Grignard precursor
P	*L*		B. p.	
5	15	$C_{10}H_{21}\cdot CN$	134—137°/20—22 mm.	C_4H_9Br
6	16	"	"	$C_5H_{11}Br$
8	16	$C_8H_{17}\cdot CN$	64/0·8 mm.	$C_7H_{15}Cl$ *

* For physical properties see Table 2*b*.

3. *Preparation of Alkyl Sulphates.*—The method, essentially that described by Dreger *et al.*,[12] employs reaction of the alcohol with a solution of chlorosulphonic acid in ether at −50°. Because of the extreme readiness of the products, especially those in which the sulphate group is near the medial position on the chain, to undergo hydrolysis, the solutions must be kept alkaline to phenolphthalein at all stages. Only the sulphates for which $P = 1$ and 2, and sodium 1-tetradecylpentadecyl sulphate ($L = 29$, $P = 15$) could be obtained in the crystalline state; the remainder were non-crystalline solids and were used as aqueous solutions. The sulphates ($P = 1$ and 2) were crystallised from water and recrystallised from aqueous butan-2-one. The tetradecylpentadecyl sulphate, obtained as a 5% emulsion in water, was dissolved in four vols. of alcohol, cooled to 25—30°, and the precipitate filtered off. The compound precipitated overnight from the filtrate was recrystallised from alcohol. The purity of the materials was assessed by Epton's method,[13] and the amount of inorganic salt was found by ashing a sample and correcting for the amount of sodium sulphate obtained from the alkyl sulphate (see Table 3).

Sodium 1-ethylnonyl sulphate was prepared as a 24% aqueous solution;[14] the remaining compounds were supplied in crystalline form containing <0·5% of inorganic salt by associates in Holland.

[12] Dreger, Keim, Miles, Shedlovsky, and Ross, *Ind. Eng. Chem.*, 1944, **36**, 610.
[13] Epton, *Trans. Faraday Soc.*, 1948, **44**, 226.
[14] Winsor, *ibid.*, 1950, **46**, 766.

Alkyl cyclo*Hexylammonium Sulphates.*—Solutions of these sulphates were prepared by shaking a 2·5% (w/w) aqueous solution of sodium alkyl sulphate and excess of 20% aqueous *cyclo*hexylammonium chloride with five successive portions of carbon disulphide (pure, for spectroscopy). The combined extracts were dried (Na_2SO_4) and filtered; the residual sodium

TABLE 2*a*.

Key no. of alkyl sulphate		Ketone			Method of reduction
P	*L*		M. p.	B. p.	
4	16	$C_{12}H_{25}\cdot CO\cdot C_3H_7$	36—37°	173—178°/24 mm.	Al *iso*propoxide
4	18	$C_{14}H_{29}\cdot CO\cdot C_3H_7$	42—45	—	,,
5	14	$C_9H_{19}\cdot CO\cdot C_4H_9$	22·6	145—146°/16 mm.	Na + C_2H_5OH
5	15	$C_{10}H_{21}\cdot CO\cdot C_4H_9$	31	120—122°/1 mm.	Al *iso*propoxide
5	19	$C_{14}H_{29}\cdot CO\cdot C_4H_9$	48—49	—	,,
6	11	$C_5H_{11}\cdot CO\cdot C_5H_{11}$ *	—	108—112°/12 mm.	H_2 (Raney nickel)
6	16	$C_{10}H_{21}\cdot CO\cdot C_5H_{11}$	35—36	127—128°/0·6 mm.	Al *iso*propoxide
6	18	$C_{12}H_{25}\cdot CO\cdot C_5H_{11}$	45	—	,,
8	15	$C_7H_{15}\cdot CO\cdot C_7H_{15}$	42·5	—	H_2 (Raney nickel)
8	16	$C_8H_{17}\cdot CO\cdot C_7H_{15}$	37·5—38	—	Al *iso*propoxide
9	17	$C_8H_{17}\cdot CO\cdot C_8H_{17}$	52—53	—	,,
10	19	$C_9H_{19}\cdot CO\cdot C_9H_{19}$	58	—	H_2 (Raney nickel)
15	29	$C_{14}H_{29}\cdot CO\cdot C_{14}H_{29}$ †	80—81	—	Al *iso*propoxide

* n_D^{20} 1·4285.

† Found: C, 82·4; H, 13·9; CO, 6·6. $C_{29}H_{58}O$ requires C, 82·5; H, 13·7; CO, 6·6%.

TABLE 2*b*.

Key no. of alkyl sulphate		Grignard precursor					
P	*L*		n_D^{20}	B. p.	Cl (found)	Cl (theory)	Aldehyde
2	10 *	$C_8H_{17}Cl$	1·4302	71°/15 mm.	23·9	23·9	$CH_3\cdot CHO$ †
2	14 *	$C_{12}H_{25}Cl$	1·4425	139°/23 mm.	17·2	17·3	,,
2	18 *	$C_{16}H_{33}Cl$	1·4513	149°/1 mm.	13·6	13·7	,,
3	14	$C_{11}H_{23}Cl$	1·4401	118°/18 mm.	18·3	18·6	$C_2H_5\cdot CHO$ †
3	15	$C_{12}H_{25}Cl$	—	—	—	—	,,
4	14	$C_{10}H_{21}Cl$	1·4377	102°/14 mm.	19·9	20·1	$C_3H_7\cdot CHO$ †
7	14	$C_7H_{15}Cl$	1·4254	49·5°/10 mm.	26·1	26·3	$C_6H_{13}\cdot CHO$

* Large-scale preparation: yield of alcohol 3—4 kg. † Not prepared in this laboratory.

TABLE 2*c*.

Key no. of alkyl suphate		Grignard precursor		
P	*L*		n_D^{20}	B. p.
7	13	$C_6H_{13}Br$	1·4478	49—55°/16 mm.
8	15	$C_7H_{15}Cl$		
9	17	$C_8H_{17}Cl$		

sulphate was washed with carbon disulphide and the washings were combined with the extract to make a total of 50 ml. of solution. With some compounds, particularly those of high molecular weight in which $P = 1$ or 2, very stable emulsions were formed. Experiments showed that (*a*) very little (<1%) of the alkyl *cyclo*hexylammonium sulphate was adsorbed on the sodium sulphate, (*b*) stable emulsions prevented the estimation of alkyl sulphates remaining in the aqueous phase. The concentration of salt in the organic phase was, therefore, determined by a modification of the methylene-blue titration method [13] by diluting an aliquot part with chloroform and titrating it against standardised cetylpyridinium bromide.

Alkyl Tri-(2-hydroxyethyl)ammonium Sulphates.—To a solution of sodium alkyl sulphate in 65% *n*-butanol a large excess (*ca.* 4-fold) of tri-(2-hydroxyethyl)ammonium sulphate was added. After being shaken, the aqueous layer was removed and the alcohol layer was washed 3 times with a little tri-(2-hydroxyethyl)ammonium sulphate. The free base was added to neutrality, and the solution was evaporated to dryness. Since molar extinction coefficients were not to be measured no precautions were taken to ensure that complete recovery of the alkyl sulphate was obtained.

In the solid state *n*-tetradecyl tri-(2-hydroxyethyl)ammonium sulphate was crystalline and the 1-propylundecyl sulphate a gum. The 1-methyltridecyl sulphate was obtained originally as a gum which became crystalline after a few days.

Infrared Measurements.—The spectra of about three-quarters of the samples were recorded from about 860 cm.$^{-1}$ to 775 cm.$^{-1}$ by means of the Grubb-Parsons S.4. double-beam spectrometer and the remainder were recorded over the same range with the Grubb-Parsons S.3. single-beam spectrometer. Spectral slit widths of 7·9 and 6·6 cm.$^{-1}$ at 831 and 790 cm.$^{-1}$ were employed, together with cell lengths of 0·021 cm. and 0·095 cm. Calculation of extinction coefficients is subject to several errors, including the titration error affecting the concentration. Values for six different solutions of *cyclo*hexylammonium 1-methyltridecyl sulphate at concentrations between 30 and 140 mmoles/l. indicate that the standard deviation of a single observation is $\pm$5·9 for an average ε of 114·2. For compounds of lower ε the standard deviation is proportionately reduced.

TABLE 3. *Analysis of alkanols, and of alkyl sulphate products made therefrom.*

Key no. of alkyl sulphate		Alcohol and properties					Yield from precursor (mol. %)	Alkyl sulphate		
								Concn. of aq. solution (% w/w)	Inorganic salt (% of alkyl sulphate)	Yield from alcohol (mol. %)
P	*L*		n_D^{20} or m. p.	B. p.	Active H found	Active H theory				
1	8	C_8H_{17}·OH †	1·42999	195—196°	—	—	—	‡	<0·1	~100
1	12	$C_{12}H_{25}$·OH †	—	141—142°/12 mm.	0·54	0·54	—	‡	0·2	—
1	14	$C_{14}H_{29}$·OH	37·4—37·7°	170°/18 mm.	—	—	76	‡	0·1	64
2	10 *	C_8H_{17}·CH(OH)·CH_3	1·4343	106°/14 mm.	0·64	0·64	79	‡	<0·1	53
2	14 *	$C_{12}H_{25}$·CH(OH)·CH_3	29—31°	159°/17 mm.	0·47	0·47	54	‡	0·2	54
2	18 *	$C_{16}H_{33}$·CH(OH)·CH_3	48—51°	156—160°/0·4 mm.	—	—	66	‡	1·0	43
3	14	$C_{11}H_{23}$·CH(OH)·C_2H_5	29·5°	150°/15 mm.	0·475	0·47	33	17·3	1·1	—
3	15	$C_{12}H_{25}$·CH(OH)·C_2H_5	37·5°	167—168°/16 mm.	0·44	0·44	48	24·0	—	—
4	14	$C_{10}H_{21}$·CH(OH)·C_3H_7	26·4°	160—161°/18·5 mm.	0·475	0·47	59	30·2	0·3	—
4	16	$C_{12}H_{25}$·CH(OH)·C_3H_7	39—40°	—	—	—	92	2·83	<0·1	55
4	18	$C_{14}H_{29}$·CH(OH)·C_3H_7	48—49°	—	0·375	0·37	85	5·1	<0·5	54
5	14	C_9H_{19}·CH(OH)·C_4H_9	27·5°	157°/17 mm.	0·475	0·47	66	19·5	1·5	—
5	15	$C_{10}H_{21}$·CH(OH)·C_4H_9	35·5—36·5°	—	0·44	0·44	83	4·75	<0·1	81
5	19	$C_{14}H_{29}$·CH(OH)·C_4H_9	54—55°	—	0·35	0·355	76	3·7	<0·5	65
6	11	C_5H_{11}·CH(OH)·C_5H_{11}	1·4355 18°	145°/53 mm.	—	—	84	5·8	3·0	34
6	16	$C_{10}H_{21}$·CH(OH)·C_5H_{11}	41°	—	—	—	82	5·2	1·1	83
6	18	$C_{12}H_{25}$·CH(OH)·C_5H_{11}	45°	192—195°/16 mm.	0·345	0·37	89	3·8	5·8	—
7	13	C_6H_{13}·CH(OH)·C_6H_{12}	38·5°	—	—	—	67	6·2	4·5	36
7	14	C_7H_{15}·CH(OH)·C_6H_{13}	42·8°	154—155°/15 mm.	0·47	0·47	—	20·4	2·0	—
8	15	C_7H_{15}·CH(OH)·C_7H_{15}	49·5°	120—124°/0·4 mm.	—	—	77	5·3	0·4	84
8	16	C_8H_{17}·CH(OH)·C_7H_{15}	49·5°	—	0·41	0·415	95	1·26	2·6	16
9	17	C_9H_{17}·CH(OH)·C_8H_{17}	59°	—	—	—	71	3·3	2·7	74
10	19	C_9H_{19}·CH(OH)·C_9H_{19}	63°	—	—	—	36	3·1	5·5	75
15	29	$C_{14}H_{29}$·CH(OH)·$C_{14}H_{29}$ §	86°	—	0·24	0·24	88	‡	0·7	47

* Large-scale preparation : yield of alcohol 3—4 kg., of alkyl sulphate 1·5—2 kg.
† Not made in this laboratory. ‡ Obtained in crystalline state.
§ Found : C, 82·1; H, 14·2. $C_{29}H_{60}O$ requires C, 82·1; H, 14·2%.

Effect of water. Water gives a broad diffuse band in the 800 cm.$^{-1}$ region, and if the drying procedure failed to remove all the moisture from the carbon disulphide solution the measured values of ε might be in error. In fact, a few spectra showed a weak band at 3400 cm.$^{-1}$ indicative of water, but solutions contained only about 0·2% of water (Karl Fischer method). Nevertheless, the extent of possible interference by water in the 800 cm.$^{-1}$ region was determined.

Solutions of isomeric tetradecyl sulphates ($P = 2$ and 7) were made in carbon disulphide solution as described; half of each solution was evaporated to dryness under vacuum at room temperature and replaced by an equal volume of dry distilled carbon disulphide. It was found that the absorption band at 3400 cm.$^{-1}$ in the untreated solution was absent from the treated solution, proving that water may indeed be present in solutions prepared by the normal procedure, and ε at the peak was decreased by $<5\%$ for both compounds. This difference is within the reproducibility of replicate determinations of ε. It may be concluded that, even if traces of water are present in the solutions examined, ε is affected only to an extent within the expected error of the observations.

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324. *Anion Exchange in Uranyl Sulphate Solution. High-concentration Effects and Rate Studies.*

By T. V. Arden and Marion Rowley.

The concentration of uranium and sulphate in anion-exchange resins in equilibrium with concentrated solutions of uranyl sulphate, UO_2SO_4, is higher than the saturation values for $UO_2(SO_4)_3^{4-}$, $UO_2(SO_4)_2^{2-}$, or $U_2O_5(SO_4)_3^{4-}$. The increase may be due to the presence of $U_2O_5(SO_4)_2^{2-}$, or more probably to the permeation of undissociated UO_2SO_4 into the resin, in addition to the normal exchange process. In dilute solution the rate of adsorption of uranium decreases with increasing pH, owing to the lower rate of diffusion through the resin of $U_2O_5(SO_4)_3^{4-}$ than $UO_2(SO_4)_3^{4-}$.

The adsorption of uranium by strongly basic anion-exchange resins from dilute acid solutions of uranyl sulphate is now well established. It has been demonstrated [1] that in dilute acid solutions (M/200, pH <2) all observations could be explained on the basis of the adsorption under equilibrium conditions of $UO_2(SO_4)_3^{4-}$ and HSO_4^- only. Increases in resin loading at higher pH were shown to be due to the presence of $U_2O_5(SO_4)_3^{4-}$. Other workers [2,3] have claimed that these increases were due to the presence of $UO_2(SO_4)_2^{2-}$, but it was considered by Arden and Wood [1] that this ion would be adsorbed only from relatively concentrated solutions. Hartley [4] observed that when uranium was adsorbed from highly concentrated solutions very high resin loadings were obtained, and the complex adsorbed appeared from analysis to be UO_2SO_4. His tentative explanation of this phenomenon assumed the formation of basic complexes of the type $UO_3SO_4^{2-}$. The same analytical results would be given by a complex $U_2O_5(SO_4)_2^{2-}$, which would complete the series suggested by Arden and Wood. Explanations of the effects of increasing pH and concentration are thus conflicting, although there is general agreement on the results obtained with dilute acid solutions. In an attempt to clarify this situation, we have studied high-concentration effects.

The experimental results already obtained would in some cases be invalidated if equilibria which had been assumed had not been attained. It has already been shown [1,5] that the rate of exchange of the uranium complex for chloride is less than that of sulphate

[1] Arden and Wood, *J.*, 1956, 1596.
[2] Grinstead, Ellis, and Olson, Paper P/522, Geneva Conference, 1955.
[3] O'Connor, ACCO 61 (U.S. Atomic Energy Commission), 1954.
[4] Hartley, Report GL/CR/CR/9, Dept. of Mines, Australia.
[5] Wood and Benham, Report CRL/AE 123, Chemical Research Laboratory.

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TABLE 1.

Solution			Observed uptake (mmoles/g.)		Observed molar ratios				Corrected uptake (mmoles/g.)		Corrected ratios		
$[UO_2^{2+}]$	$[SO_4^{2-}]$	pH	UO_2	SO_4	$\frac{SO_4}{UO_2}$	$\frac{Cl}{UO_2}$	$\frac{Cl}{SO_4}$	P *	UO_2	SO_4	$\frac{SO_4}{UO_2}$	$\frac{Cl}{UO_2}$	$\frac{Cl}{SO_4}$
0·0066	0·0081	3·59	1·095	—	—	3·30	—	—	1·09	—	—	3·36	—
0·0166	0·0203	3·37	1·26	2·82	2·24	2·92	1·30	0·01	1·27	2·81	2·22	2·89	1·31
0·0331	0·0406	3·19	1·38	—	—	2·66	—	0·02	1·36	—	—	2·70	—
0·0663	0·0812	3·00	1·52	3·08	2·03	2·42	1·29	0·04	1·48	3·04	2·05	2·48	1·21
0·133	0·162	2·72	1·73	—	—	2·12	—	0·07	1·66	—	—	2·21	—
0·331	0·406	2·40	2·00	3·49	1·74	1·83	1·05	0·19	1·81	3·30	1·82	2·03	1·11
0·442	0·609	2·20	2·11	—	—	1·73	—	0·26	1·85	—	—	1·98	—
0·663	0·812	2·10	2·28	3·74	1·64	1·59	0·97	0·40	1·88	3·34	1·77	1·96	1·10
0·828	1·015	1·97	2·40	—	—	1·52	—	0·51	1·89	—	—	1·94	—
0·994	1·218	1·89	2·45	3·93	1·60	1·48	0·93	0·61	1·84	3·32	1·81	1·99	1·11
1·160	1·421	1·75	2·57	—	—	1·41	—	0·71	1·86	—	—	1·98	—
1·325	1·624	1·71	2·64	4·14	1·52	1·33	0·88	0·86	1·78	3·28	1·84	2·05	1·12

* Permeation correction, see p. 1712.

TABLE 2. pH 1·86.

Time (min.)	Quantity sorbed				Concentration			Charge			
	UO_2	SO_4	Cl	$\frac{Cl}{SO_4}$	$\{UO_2\}_1$	$\{UO_2\}_2$	$\{SO_4\}_t$	$(UO_2)_1$	$(UO_2)_2$	$(SO_4)_t$	Total
1	0·143	0·907	1·52	1·68	0·143	—	0·478	0·57	—	0·95	1·52
2	0·213	1·23	2·01	1·64	0·213	—	0·59	0·85	—	1·18	2·03
5	0·293	1·83	3·04	1·66	0·293	—	0·95	1·17	—	1·90	3·07
10	0·418	2·20	3·61	1·64	0·418	—	0·95	1·67	—	1·90	3·57
30	0·577	2·42	3·66	1·48	0·577	—	0·69	2·30	—	1·38	3·68
60	0·691	2·53	3·70	1·46	0·691	—	0·45	2·76	—	0·90	3·66
120	0·772	2·63	3·72	1·42	0·772	—	0·31	3·09	—	0·62	3·71
240	0·914	2·76	3·74	1·38	0·914	—	0·02	3·65	—	0·04	3·69
360	0·924	2·74	3·78	1·38	0·924	—	−0·02	3·70	—	—	3·70
480	0·935	2·82	3·80	1·37	0·935	—	0·02	3·74	—	—	3·74
960	0·957	2·88	3·83	1·34	0·957	—	0·01	3·82	—	—	3·82
1440	0·965	2·88	3·86	1·34	0·965	—	−0·01	3·85	—	—	3·85
					TABLE 3. pH 3·60.						
1	0·153	0·832	1·38	1·66	0·15	0	0·41	0·60	0	0·82	1·42
2	0·200	1·12	1·83	1·63	0·20	0	0·51	0·80	0	1·02	1·82
5	0·341	1·68	2·69	1·60	0·33	0·01	0·68	1·32	0·02	1·36	2·70
10	0·42	2·05	3·23	1·58	0·42	0	0·75	1·68	0	1·50	3·18
30	0·56	2·35	3·67	1·57	0·47	0·09	0·80	1·88	0·18	1·60	3·66
60	0·745	2·49	3·67	1·48	0·55	0·20	0·52	2·20	0·40	1·04	3·64
120	0·910	2·63	3·69	1·40	0·66	0·25	0·24	2·64	0·50	0·48	3·62
240	1·10	2·74	3·75	1·37	0·69	0·41	0·07	2·76	0·82	0·14	3·72
360	1·10	2·80	3·78	1·46	0·71	0·39	0·08	2·84	0·78	0·16	3·78
480	1·11	2·84	3·82	1·35	0·75	0·36	0·04	3·00	0·72	0·08	3·80
960	1·13	2·88	3·84	1·33	0·79	0·34	0	3·16	0·68	0	3·84
1440	1·14	2·91	3·89	1·33	0·79	0·35	0	3·16	0·70	0	3·86
					TABLE 4. pH 4·45.						
1	0·104	0·669	1·25	1·87	0	0·104	0·57	—	0·21	1·08	1·29
2	0·156	1·03	1·95	1·89	0	0·156	0·86	—	0·31	1·72	2·03
5	0·240	1·58	2·94	1·86	0	0·240	1·25	—	0·48	2·50	2·98
10	0·297	1·82	3·32	1·83	0·02	0·28	1·33	0·08	0·56	2·66	3·30
30	0·454	2·08	3·67	1·76	0·05	0·40	1·34	0·20	0·80	2·68	3·68
60	0·570	2·19	3·68	1·68	0·13	0·44	1·11	0·52	0·88	2·22	3·62
120	0·780	2·35	3·68	1·57	0·24	0·54	0·79	0·96	1·08	1·58	3·62
240	0·981	2·50	3·70	1·48	0·32	0·66	0·55	1·28	1·32	1·10	3·70
360	1·08	2·57	3·72	1·44	0·34	0·74	0·45	1·36	1·48	0·90	3·74
480	1·17	2·61	3·72	1·42	0·33	0·84	0·37	1·32	1·68	0·74	3·74
960	1·32	2·70	3·75	1·38	0·33	0·99	0·21	1·32	1·98	0·41	3·71
1440	1·45	2·80	3·80	1·36	0·35	1·10	0·10	1·40	2·20	0·20	3·80
					TABLE 5. pH 4·95.						
1	0·082	0·890	1·65	1·96	0·05	0·03	0·69	0·20	0·06	1·38	1·64
2	0·108	1·20	2·20	1·84	0·09	0·02	0·90	0·36	0·04	1·80	2·20
5	0·166	1·58	2·94	1·74	0·05	0·12	1·24	0·20	0·24	2·48	2·92
10	0·222	1·82	3·35	1·84	0·07	0·16	1·38	0·28	0·32	2·76	3·36
30	0·370	2·06	3·64	1·75	0·09	0·28	1·33	0·36	0·56	2·66	3·58
60	0·500	2·14	3·67	1·72	0·11	0·39	1·22	0·44	0·78	2·44	3·66
120	0·686	2·26	3·70	1·62	0·13	0·56	1·03	0·52	1·12	2·06	3·70

or bisulphate. Recent work [6] has shown that the rate of uptake of uranium decreases with increasing pH. These phenomena have now been examined in more detail.

Experimental

The resins used were samples of De-Acidite FF having capacities of 3·67 and 3·85 mequiv./g., and weight swelling * (in the chloride form) of 0·60 g./g. For the saturation tests, a solution of uranyl sulphate was prepared containing 1·325M-uranyl ion and 1·624M-sulphate ion at pH 1·71. This was diluted to various concentrations down to 0·0066M UO_2^{2+}. Samples of approx. 2 g. of moist resin were placed in centrifuge tubes closed with sintered discs, and a large excess of each test solution passed during several hours. The liquor was then centrifuged off, and the adsorbed uranium and sulphate were eluted from the resin with a solution containing 0·9M-sodium chloride and 0·1M-hydrochloric acid and were analysed by standard methods. The resins were finally reconverted into the chloride form before being dried and weighed. A correction for the residual interstitial liquor, amounting to 0·03 ml. of liquor per g. of dry resin chloride, was made by Kraus and Moore's method.[7] The results are given in cols. 1—5 of Table 1.

The water contents of the centrifuged resins after equilibration were measured in separate tests, and found to vary from 0·58 g. per g. of dry resin chloride at 0·33M to 0·56 g. per g. at 1·2M. The specific gravities of the test solutions varied linearly with concentration of uranyl sulphate from 1·00 at zero to 1·414 at 1·21M.

For the rate measurements, two techniques were used according to the total time involved. For periods of 30 min. or more the resin sample, initially in the chloride form, was agitated continuously at 25° with a large excess of test solution, and was then washed with the same solution into a centrifuge tube. As soon as the whole of the resin had been transferred it was drained under vaccum, and then centrifuged. The time was measured from the first contact of resin and solution to the moment of sucking dry. For times of less than 30 min. this procedure was insufficiently accurate, and the centrifuge tube was used as a filter throughout. The test solution was passed at a rate of 260 ml:/min., giving a residence time of only 0·23 sec. At this high rate, the concentration of the liquor was not significantly altered by its passage through the resin, and it has been assumed that the resin was in contact with a solution of constant composition. The times were measured from the first application of liquor to the moment of sucking dry; and the resin was then centrifuged as above before elution and analysis.

The solutions used contained 0·0106M-uranyl ion and 0·0322M-sulphate, the pH values being adjusted to 1·86, 3·60, 4·45, and 4·95 by means of sodium hydroxide in four separate tests. The solution at pH 4·95 was metastable, and it was found impossible to continue the test for more than 2 hr. In the other three cases measurements were made up to 24 hr.

Columns 2—4 of Tables 2—5 give the quantities of uranyl and sulphate ion adsorbed, and chloride desorbed (each as mmoles per g. of dry resin chloride) after various periods. The significance of the remaining columns is discussed below.

Discussion

Adsorption from Concentrated Solution.—The results in Table 1 show that resin loadings increase rapidly with increasing concentration of uranyl sulphate in solution. When this exceeds 0·133M the loading is above the saturation value for $UO_2(SO_4)_2^{2-}$ or $U_2O_5(SO_4)_3^{4-}$, the highest figure recorded being almost double this value. This observation, which is in agreement with Hartley's, could result from the adsorption of $U_2O_5(SO_4)_2^{2-}$, and it is clear that mixtures on the resin of this ion with $UO_2(SO_4)_2^{2-}$ could give results agreeing approximately with the observed figures.

From mass-action considerations, high solution concentrations would be expected to favour the adsorption of these bivalent complexes, in competition with the quadrivalent ions. Nevertheless, the experimental results diverge sufficiently from the theoretical figures [$U_2O_5(SO_4)_2^{2-}$ requires molar ratios SO_4/UO_2 1·0, Cl/UO_2 1·0, Cl/SO_4 1·0; $UO_2(SO_4)_2^{2-}$ requires SO_4/UO_2 2·0, Cl/UO_2 2·0, Cl/SO_4 1·0] to suggest that this postulation can at best be only partly correct.

* Measured by Pepper's technique (*J. Appl. Chem.*, 1951, 124).

[6] Napier, personal communication.

[7] Kraus and Moore, *J. Amer. Chem. Soc.*, 1953, **75**, 1497.

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The measured uptakes of uranium and sulphate include the quantities due to the permeation of undissociated UO_2SO_4 into the resin beads. It was shown by Betts and Michels [8] that uranyl sulphate is strongly associated in acid solution. Although our tests differ from theirs in that higher concentrations of uranyl sulphate have been used, with less free acid, it is considered that their conclusions would apply to an equal or greater extent to the most concentrated solutions of Table 1. The water content and specific gravities were used to calculate the quantity of uranyl sulphate which would be present inside the resin beads, on the assumption that the concentration in the water in the gel is identical with that in the surrounding solution. The results of this calculation are given in column 9 of Table 1 (*P*). The basis of calculation becomes less justifiable

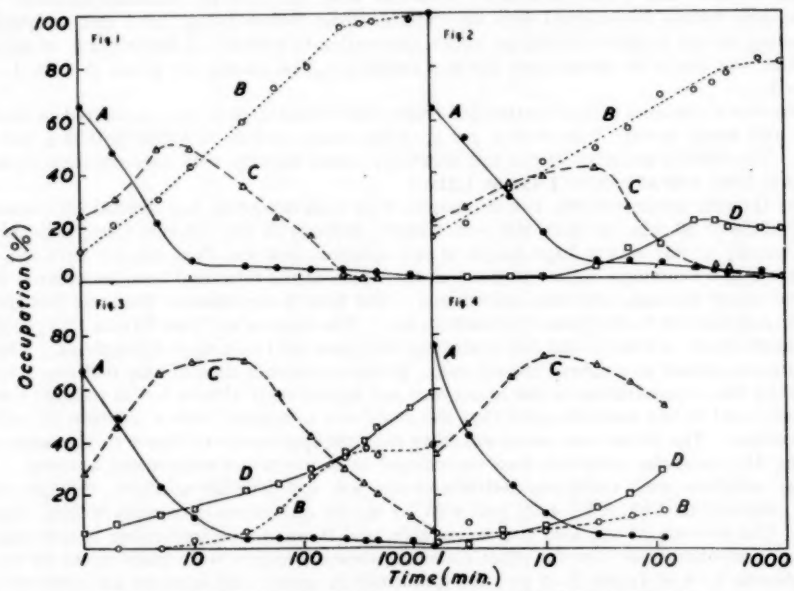

FIG. 1, pH 1·86; FIG. 2, pH 3·6; FIG. 3, pH, 4·45; FIG. 4, pH 4·95.
A, Cl^-; *B*, $UO_2(SO_4)_3^{4-}$; *C*, SO_4^{2-}; *D*, $U_2O_5(SO_4)_3^{4-}$.

with decreasing concentration in solution, and the corrections in col. 9 become correspondingly too large. As, however, the figures themselves decrease rapidly with concentration, the errors in them will not be large.

The corrected ratios SO_4/UO_2 and Cl/UO_2 rise, and the ratio Cl/SO_4 falls, with increasing concentration up to 0·33M, after which constant values of 1·8, 2·0, and 1·1 respectively are maintained up to the highest concentration which could be achieved without crystallisation. These constant values suggest the presence of one ion only, since values for a mixture of ions would normally change with varying solution conditions.

The calculated values are not in exact agreement with those required for any ion which has been postulated, and it is clear that the factors governing equilibrium in highly concentrated solutions are not completely understood. The ion which most closely corresponds with the calculated ratios is $UO_2(SO_4)_2^{2-}$, and it is considered that the enhanced resin loadings observed by Hartley and ourselves in concentrated solution can best be explained by postulating the permeation of UO_2SO_4 into resin already saturated with $UO_2(SO_4)_2^{2-}$.

[8] Betts and Michels, *J.*, 1949, S 286.

The variations of uranium adsorption can thus be explained as follows. In dilute acid solution (M/200, pH <2), the only ions adsorbed to a measurable extent are $UO_2(SO_4)_3^{4-}$ and HSO_4^-, the adsorption of the latter decreasing to zero as the pH rises to 2·0. Increase in pH at the same concentration causes adsorption of $U_2O_5(SO_4)_3^{4-}$. Increase in concentration at low pH favours the adsorption of $UO_2(SO_4)_2^{2-}$, which displaces all other ions at concentrations greater than 0·3M in solution. It is to be expected that a combination of high pH and high concentration would favour adsorption of $U_2O_5(SO_4)_2^{2-}$, but these conditions cannot be achieved experimentally.

Rate Tests.—Comparison of the uranium uptake figures in Tables 2—5 shows that the initial rate of sorption is greatest below pH 4·0 and decreases with increasing pH in agreement with Napier's observations. The value Cl/SO_4 tends in each case to a final figure of 1·33, suggesting that at equilibrium a mixture of $UO_2(SO_4)_3^{4-}$ and $U_2O_5(SO_4)_3^{4-}$ is present on the resin. If, following Arden and Wood's reasoning, it is assumed that before equilibrium is reached these two ions are present, together with free SO_4^{2-}, the concentration of each ion may be calculated as follows: Let $\{UO_2\}_m$ and $\{SO_4\}_m$ represent the measured quantities sorbed, and $\{Cl\}_m$ the measured quantity desorbed, each as mmoles per g. of dry resin chloride, and let $\{SO_4\}_f$, $\{UO_2\}_1$, and $\{UO_2\}_2$ represent respectively the quantities of free sulphate and of uranium sorbed as $UO_2(SO_4)_3^{4-}$ and $U_2O_5(SO_4)_3^{4-}$ (as mmoles of UO_2 per g. of dry resin chloride).
Then

$$\{UO_2\}_1 + \{UO_2\}_2 = \{UO_2\}_m$$
$$3\{UO_2\}_1 + 1{\cdot}5\{UO_2\}_2 + \{SO_4\}_f = \{SO_4\}_m$$
$$4\{UO_2\}_1 + 2\{UO_2\}_2 + 2\{SO_4\}_f = \{Cl\}_m$$

Whence

$$\{UO_2\}_1 = 2\{SO_4\}_m - \{Cl\}_m - \{UO_2\}_m$$
$$\{UO_2\}_2 = 2\{UO_2\}_m - 2\{SO_4\}_m + \{Cl\}_m$$
$$\{SO_4\}_f = 1{\cdot}5\{Cl\}_m - 2\{SO_4\}_m$$

The calculated values for $\{UO_2\}_1$, $\{UO_2\}_2$, and $\{SO_4\}_f$ are given in Tables 2—5, together with the total negative charges associated with each of these ions. From these results the percentage of active groups occupied by each of these ions and by chloride have been calculated, the results being plotted in Figs. 1—4. These results show that, initially, uranium complexes and sulphate are simultaneously adsorbed by the resin in exchange for chloride, after which the free sulphate gradually disappears, being replaced by complex.

The rate of adsorption of the higher complex is considerably slower than that of $UO_2(SO_4)_3^{4-}$, whose adsorption is substantially complete in all tests after about 300 minutes. At pH 3·6, when the proportion of $U_2O_5(SO_4)_3^{4-}$ adsorbed is small, its maximum concentration is reached in approximately the same time, but at pH 4·45, when the greater proportion of the active groups become occupied by the higher complex, its concentration is still rising steadily after 24 hours, the replacement of free sulphate being correspondingly incomplete. At pH 4·95 the rate of fall of free sulphate is still lower in the region tested. It follows that the rate of adsorption of $U_2O_5(SO_4)_3^{4-}$ decreases as its final concentration increases, suggesting that the adsorption of the larger anion in the outer layers of the resin particles causes steric interference with the further penetration into the interior of the resin molecule. It is not possible to interpret the rate data quantitatively, since the method of calculation of Tables 2—5 considerably exaggerates minor analytical errors. It must be considered that Figs. 1—4 give only approximate representations of the mechanism of the adsorption process. Quantitative elucidation will require a technique, such as absorption spectrography in the solid phase, which permits direct measurements of the concentration of each ion in the resin.

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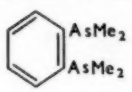
325. *Complexes of Bivalent Nickel with Some Compounds containing Two Sulphide Chelate Groups.*

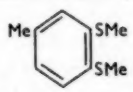
By R. Backhouse, M. E. Foss, and R. S. Nyholm.

The complexes formed by the bis-sulphides (di-thioethers), 1 : 2-diethylthioethane (III) and 1 : 2-dimethylthioethane (IV), with bivalent nickel halides and with nickel perchlorate have been prepared and studied. The halides form complexes of the type $[Ni(Chelate)_2(Hal)_2]^0$ but the perchlorate gives rise to the tris-chelate complex, $[Ni(Chelate)_3][ClO_4]_2$. The compounds are not very stable, being decomposed by water, alcohol, or acetone. Measurements of conductivity (in nitrobenzene), molecular weight (in chloroform), and magnetic susceptibility indicate that in all cases the nickel atom is octahedrally co-ordinated. Attempts to obtain complexes of higher valency states of nickel were not successful. The nature of the bonding in these bivalent nickel complexes is discussed.

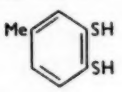
For comparison with earlier studies on the stabilisation of various valency states of nickel with an alkyl tritertiary [1] and an aryl [2-5, cf. 6] ditertiary arsine (I), the behaviour of bis-sulphide chelate groups has been investigated. It was hoped to overcome the relatively poor co-ordinating ability of sulphides towards nickel by using a bis-sulphide chelate group. Accordingly, for comparison with (I), 4-methyldithioveratrole (II) was prepared and its behaviour investigated. Only minute amounts of unstable bromo- and iodo-complexes of nickel were obtained with the latter and the use of this chelate group was therefore abandoned in favour of wholly alkyl bis-sulphides which form more stable complexes. In particular 1 : 2-diethylthioethane (III) and 1 : 2-dimethylthioethane (IV)



(I)



(II)



(V)

(III) $C_2H_5{\cdot}S{\cdot}[CH_2]_2{\cdot}S{\cdot}C_2H_5$ $CH_3{\cdot}S{\cdot}[CH_2]_2{\cdot}S{\cdot}CH_3$ (IV)

have been prepared and studied. Complexes of chelate groups of this type have been prepared by Morgan and Ledbury [7] with salts of certain metals but the only nickel complex previously studied was the thiocyanate, which was prepared by Tschugaeff [8] and by Bennett *et al.*[9] The former assigned an octahedral configuration to the nickel atom on the basis of the analysis but no previous physical measurements have been reported.

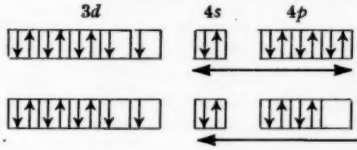
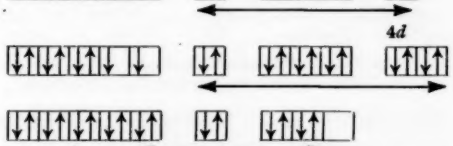
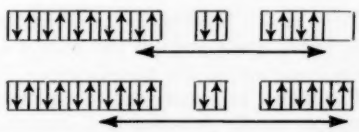
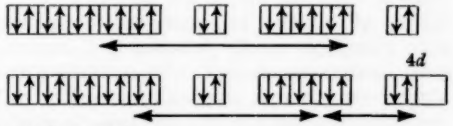
The stereochemistry of nickel complexes has been discussed elsewhere,[10-12] and Table 1 is given as a basis for the interpretation of the magnetic and cryoscopic data given later. It should be emphasised that quadricovalent, spin-free complexes are rare; if tetrahedral, a large orbital contribution to the moment is expected [13,14] and hence magnetic data are useful as a guide to the stereochemistry. However, in all compounds studied here the nickel atom is sexacovalent. In the spin-free complexes the outer bonding orbitals which are required for the stereochemistry discussed are shown but the evidence for their use is presumptive,

[1] Barclay and Nyholm, *Chem. and Ind.*, 1953, 378.
[2] Nyholm, *J.*, 1950, 2061.
[3] Nyholm, *J.*, 1951, 2602.
[4] Nyholm, *J.*, 1952, 2906.
[5] Nyholm and Short, *J.*, 1953, 2670.
[6] Jensen, *Z. anorg. Chem.*, 1936, **229**, 265.
[7] Morgan and Ledbury, *J.*, 1922, **121**, 2882.
[8] Tschugaeff, *Ber.*, 1908, **41**, 2222.
[9] Bennett, Mosses, and Statham, *J.*, 1930, 1668.
[10] Nyholm, *Chem. Rev.*, 1953, **53**, 263.
[11] Jörgensen, *Acta Chem. Scand.*, 1955, **9**, 1362.
[12] Orgel, *Report to the Xth Solvay Council*, Brussels, 1956.
[13] Nyholm, *J. Proc. Roy. Soc., N.S.W.*, 1955, **89**, 1.
[14] Nyholm, *Report to the Xth Solvay Council*, Brussels, 1956.

and theoretical rather than experimental. Whether they are occupied or not is irrelevant for *this* discussion of the shape of the molecule.

The nickel(II) complexes with 1 : 2-diethylthioethane were prepared by treating a concentrated alcoholic solution of the nickel salt with the chelate group. The iodide crystallised out spontaneously and, probably owing to low solubility, is the most stable. To obtain the chloride, however, the solution had to be evaporated to a very small volume and set aside. On the other hand, the derivatives of 1 : 2-dimethylthioethane separated immediately on the addition of the chelate group. Presumably owing to their higher solubility in alcohol, the derivatives of the diethyl chelate group are obtained in analytically less pure condition than those of the dimethyl chelate. The difficulty of removing traces of nickel halide from the former is reflected in the analytical figures. The perchlorate was

TABLE 1. *Electronic arrangement, stereochemistry, and magnetic properties of bivalent nickel complexes.*

Type of complex	Co-ordination no. of Ni(II) atom	Probable electronic configuration (3d, 4s, 4p)
Spin	4	
Free	6	
Spin	4	
Paired	6	

Type of complex	Arrangement of bonds	Expected magnetic moment (B.M.)	Example
Spin	Tetrahedral	>3·5	$[Ni(NO_3)_2,2(C_2H_5)_2P]$[a] ($\mu_{eff.}$ = 3·05 B.M.) [a]
	Square	3·1—3·3	3·1—3·3
Free	Octahedral	3·1—3·3	$[Ni(Dipyridyl)_3][ClO_4]_2$ ($\mu_{eff.}$ = 3·10 B.M.) [b]
Spin	Square	Diamagnetic	$[NiCl_2,2(C_2H_5)_2P]$[a] ($\mu_{eff.}$ = diamagnetic) [a]
Paired	Octahedral	Diamagnetic	$[Ni(Diarsine)_3][ClO_4]_2$ (solid) ($\mu_{eff.}$ = diamagnetic) [c]

[a] See ref. 15. [b] Burstall and Nyholm, *J.*, 1952, 3570. [c] See ref. 2. ⟷ Bond orbitals.

the most difficult of the complexes to obtain, and in this case it was necessary to remove all the alcohol by storage in a desiccator over calcium chloride. In all cases where evaporation was required the product was contaminated with the original nickel salt which is difficult to remove without partial decomposition of the complex—even in the case of the iodide. The physical properties and the experimentally determined magnetic moments of the complexes are shown in Table 2. The low solubilities of the complexes prevented any determination of molecular weights in the case of the ethyl derivatives but two measurements on methyl complexes are given which indicate six-fold co-ordination in chloroform.

[15] Asmussen, "Magnetokemiske Undersogelser over Uorganiske Kompleksforbindelser," Copenhagen, 1944, p. 221.

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In all cases the conductivity measurements indicate six-fold co-ordination. The magnetic measurements all indicate two unpaired electrons with a small orbital contribution. The complexes are therefore of the " outer orbital " type and, in the light of the discussion above, octahedrally co-ordinated.

All attempts to isolate complexes of the type $[Ni(Chelate)_3][Hal]_2$ were unsuccessful, only the perchlorate of the trischelate cation being isolated. In an attempt to ascertain whether any appreciable amounts of $[Ni(Chelate)_3]Br_2$ were formed in solution, the compound $[Ni(1 : 2\text{-dimethylthioethane})_2Br_2]^0$ in nitrobenzene was treated with excess of the chelate group. There was no change in the very low conductance of the solution, showing that electrolytes were not being formed.

It is of interest to know why these sulphur chelate groups are so much less effective than the tertiary arsine ones in effecting electron pairing and in forming complexes with strong " inner orbital " binding. It has been suggested [16] that the two factors of prime

TABLE 2.

Complex *	Formula weight	Colour	*M*, in boiling $CHCl_3$	Magnetic moment (B.M.) (25°)	Molecular conductivity in $PhNO_2$ (Concn. $\simeq$ 0·001M)
$Ni(ET)_2Cl_2$	430	Green	—	3·21	Non-electrolyte †
$Ni(ME)_2Br_2$	463	Green	458, 432	3·21	Non-electrolyte
$Ni(ET)_2Br_2$	519	Green	—	3·20	Non-electrolyte
$Ni(ME)_2I_2$	557	Yellow	555, 568	3·22	Non-electrolyte
$Ni(ET)_2I_2$	613	Yellow	—	3·12	Non-electrolyte
$[Ni(ME)_3](ClO_4)_2$...	708	Blue	—	3·16	41·5 mhos ‡

* ET = 1 : 2-Diethylthioethane (III); ME = 1 : 2-Dimethylthioethane (IV).
† " Non-electrolyte " means Λ_M <0·5 mho. ‡ Concentration is M/28,000.

importance in strong binding to transition metals are (i) the *effective* electronegativity of the ligand donor atom and (ii) the extent of d_π bonding between the metal and ligand using d_ϵ electron pairs of the metal atom. There has been some confusion concerning the ability of sulphur to cause electron pairing; sulphur readily effects electron pairing with transition metals *provided* it is bicovalent. Thus chelate groups of the type (V) co-ordinate very strongly with transition metals [17] but with sulphides the co-ordinating ability is much less; in passing from RS^- to R·SR the proton affinity of the sulphur atom has decreased enormously, this being a rough measure of tendency to form strong σ bonds. Since chelate groups such as *o*-phenylenebisdimethylarsine (I), which have practically no basic properties, will co-ordinate strongly with transition metals, it has been suggested that it is the double bonding which in the case of the arylarsine chelate groups causes the formation of strong complexes. We conclude that both dialkyl and alkyl aryl sulphides, even if present in chelate groups, are reluctant to form d_π bonds with transition metals. It is conceivable that the reason for this is one of size, the necessary vacant *d* orbital of the bicovalent sulphur atom failing to overlap sufficiently with the filled d_ϵ orbital of the metal.

EXPERIMENTAL

Chelate Groups.—1 : 2-Dimethylthioethane was prepared according to the method of Morgan and Ledbury.[7] The 1 : 2-diethylthioethane was made in a similar manner from ethanethiol and ethylene dibromide. The purified product boils at 211°.

Bis-(1 : 2-dimethylthioethane)dichloronickel(II).—Nickel chloride hexahydrate (1·8 g.), dissolved in the minimum volume of alcohol, was treated with the chelating agent (1·85 g.) and the green product which separated (1·9 g.) was washed with alcohol and ether (Found : C, 25·7; H, 5·4; Ni, 15·7. $C_8H_{20}Cl_2S_4Ni$ requires C, 25·7; H, 5·36; Ni, 15·7%). On heating, the *compound* decomposes at 180° without melting. It is decomposed by cold water and boiling ethanol. The complex is slightly soluble in chloroform but practically insoluble in alcohol, benzene, ether, or nitrobenzene. Owing to decomposition in hot chloroform, ebullioscopic determination of the molecular weight was not possible.

[16] Kabesh and Nyholm, *J.*, 1951, 3245.
[17] Sandell " Colorimetric Determination of Traces of Metals," Interscience, London, 1950, p. 130.

Bis-(1 : 2-*dimethylthioethane*)*dibromonickel*(II).—This was prepared as for the corresponding chloride by use of nickel bromide trihydrate (1·4 g.) and the chelate group (1·25 g.); yield 2·05 g. (Found : C, 21·1; H, 4·4; S, 28·0; Ni, 12·6%; *M*, ebullioscopic in $CHCl_3$ in 0·63% solution, 432, in 1·19% solution, 458. $C_8H_{20}Br_2S_4Ni$ requires C, 20·8; H, 4·32; S, 27·7; Ni, 12·7%; *M*, 463). The bright green *compound* melts at 207° (decomp.). Like the chloride, it is only slightly soluble in most solvents but in chloroform it dissolves sufficiently to permit of molecular-weight measurements.

Bis-(1 : 2-*dimethylthioethane*)*di-iodonickel*(II).—This was prepared as for the corresponding chloride and bromide from nickel iodide (1·56 g.) and the chelating agent (1·3 g.), the *compound* separating immediately as bright yellow crystals (2·2 g.) (Found : C, 17·2; H, 3·8; Ni, 10·3%; *M*, ebullioscopic in $CHCl_3$ in 0·73% solution, 555, in 0·56% solution, 568. $C_8H_{20}I_2S_4Ni$ requires C, 17·2; H, 3·6; Ni, 10·5%; *M*, 557). On heating, the compound melts at 187° (decomp.).

Iodine Oxidation Product of $[(Ni(Chelate)_2I_2]^0$.—Bis-(1 : 2-dimethylthioethane)di-iodonickel(II) (2·8 g.), prepared as above, was dissolved in chloroform (100 ml.) and treated with iodine (1·5 g.), black needles (2·9 g.) separating immediately (Found : C, 11·95; H, 2·6; Ni, 7·71. $C_8H_{20}I_4S_4Ni$ requires C, 11·8; H, 2·46; Ni, 7·21%). Since the magnetic moment indicated two unpaired electrons ($\mu_{eff.}$ = 2·96 B.M.) and hence a bivalent nickel atom, the *complex* is apparently a polyiodide of bivalent nickel and hence it was not further investigated : chlorine and bromine were also tried as oxidants but caused decomposition of the complexes.

Bis-(1 : 2-*diethylthioethane*)*dichloronickel*(II).—Nickel chloride hexahydrate (1·8 g.) in alcohol was treated with the chelating agent (2·0 g.), and the green solution concentrated to 5 ml. by heating and stored in a desiccator. Green crystals separated, consisting of the *complex* contaminated with nickel chloride. These were filtered off and washed with a small amount of absolute alcohol (Found : C, 32·4; H, 6·3; Ni, 14·2. $C_{12}H_{28}Cl_2S_4Ni$ requires C, 32·4; H, 6·57; Ni, 13·7%); m. p. 116—118° (decomp.). The complex is decomposed in the cold by alcohol, acetone, and water and undergoes slow decomposition in the solid state.

Bis-(1 : 2-*diethylthioethane*)*dibromonickel*(II).—Nickel bromide trihydrate (1·4 g.) in alcohol was treated with the chelating agent (1·5 g.) and the product worked up as above. The green crystals of the *bromide* (2·0 g.) were filtered off and purified by washing with absolute alcohol (Found : C, 27·2; H, 5·25; Ni, 11·2. $C_{12}H_{28}Br_2S_4Ni$ requires C, 27·77; H, 5·44; Ni, 11·32%).

Bis-(1 : 2-*diethylthioethane*)*di-iodonickel*(II).—Nickel iodide hexahydrate (1·6 g.) in alcohol (20 ml.) was treated with the thio-ether (1·5 g.), the solution turning yellow immediately and depositing golden-yellow crystals (2·0 g.) of the required *complex*, which darkened on standing (Found : C, 23·5; H, 4·6; Ni, 9·4. $C_{12}H_{28}I_2S_4Ni$ requires C, 23·51; H, 4·60; N, 9·58%). The compound melts at 177·9° (decomp.). It is more stable than the bromide and chloride, presumably owing to its lower solubility.

Tris-(1 : 2-*diethylthioethane*)*nickel*(II) *Perchlorate*.—Nickel perchlorate hexahydrate (2 g.) in alcohol (10 ml.) was treated with the sulphide (2·6 g.). The green solution was stored in a vacuum desiccator over calcium chloride, to remove the alcohol. The residue, containing the blue crystals of the *complex* together with nickel perchlorate, was washed with absolute alcohol (3—4 ml.) at 0° and then with a minimum of ether (Found : C, 29·4; H, 5·5; Ni, 8·4. $C_{18}H_{42}O_8Cl_2S_6Ni$ requires C, 30·5; H, 5·98; Ni, 8·29%). On heating, the compound darkens at 154° and decomposes at 172—176°. The perchlorate is much less stable and is more soluble than the corresponding halides. It is readily decomposed by alcohol, acetone, and water.

Attempts to form the quadricovalent nickel(II) compound $[Ni(Chelate)_2][ClO_4]_2$ by treating nickel perchlorate with two mols. of chelate group were unsuccessful. The product always consisted of the tris-form contaminated with large amounts of nickel perchlorate, and most of the complex decomposed before all the nickel perchlorate could be removed by washing with alcohol.

Analysis.—Nickel was determined by destroying the organic material of the complex with concentrated sulphuric acid containing 70% perchloric acid (0·1 ml.), the nickel then being estimated electrolytically. An alternative method used in some cases involving simple ignition to nickel oxide gave similar results. Some carbon, hydrogen, and sulphur microanalyses were carried out by Dr. E. Challen. Magnetic susceptibilities were determined by the Gouy method.

N.S.W. University of Technology,
Sydney, Australia.
Sir William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1.
Technical College, Gloucester.

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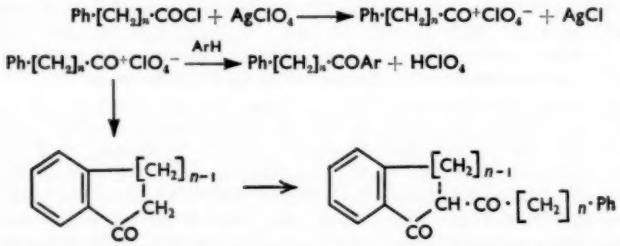
326. *Acylation and Allied Reactions Catalysed by Strong Acids. Part XVI.* The Reactions of Some ω-Phenylalkanoyl Perchlorates.*

By H. Burton and D. A. Munday.

The ω-phenylalkanoyl perchlorates when suitably constituted exhibit both inter- and intra-molecular acylating activity as well as concurrent β-diketone formation in nitromethane solution. The reactions proceed less well in methyl, phenyl, or benzyl cyanide and this is ascribed to solvation of the perchlorates. The acetylation of some cyclic ketones is also described.

The insoluble nature of the ketone–catalyst complex produced in Friedel–Crafts acylations with catalysts such as aluminium chloride generally prevents further attack on the ketone by the acylating agent. However, in the simplified Friedel–Crafts-type reaction in which silver perchlorate and an acyl halide are used to produce silver chloride and acyl perchlorate, the latter acting as a source of carbonium ions,[1–4] this is not so, and it should be possible for the product first formed to undergo further acylation. In experiments with phenylalkanoyl perchlorates, $Ph\cdot[CH_2]_n\cdot CO\cdot ClO_4$ ($n = 2$—4), we have found this to be the case.[5] Cyclic ketones and diketones, as well as open-chain ketones formed by competitive reaction with a reagent such as toluene or anisole, are obtained:



Indan-1-one (0·30 mole) and 2-β-phenylpropionylindan-1-one (0·23 mole) are produced readily at 0° from β-phenylpropionyl perchlorate (1 mole) in nitromethane solution. In toluene alone, 0·55 mole of *p*-β-phenylpropionyltoluene is produced together with 0·09 mole of indan-1-one, whereas in a mixture of nitromethane and toluene (2 moles) the higher dielectric constant favours cyclisation and 0·20 mole of indan-1-one, 0·06 mole of diketone, and only 0·40 mole of the open-chain ketone are formed. In the presence of the more reactive anisole the product is exclusively *p*-β-phenylpropionylanisole.

When $n = 4$ similar results are obtained, but only 0·10 mole of 1 : 2-benzosuberone is produced even with a longer reaction time. This is in accordance with the 4 : 1 ratio for yields of indan-1-one and 1 : 2-benzosuberone obtained by the action of aluminium chloride on the corresponding halides.[6] Some diketone material is also formed, as is indicated by the violet colour produced when an alcoholic solution of the reaction product is treated with aqueous ferric chloride, and also by the formation of a viscous copper derivative; but so far we have been unable to isolate the pure diketone. In toluene no cyclisation was observed at all and only 0·01 mole of the straight-chain ketone was formed, indicating the diminishing reactivity of the carbonium ion as *n* increases. However, with the markedly more nucleophilic anisole a quantitative yield of *p*-δ-phenylvalerylanisole confirmed the

* Part XV, *J.*, 1956, 3933.

[1] Mackenzie and Winter, *Trans. Faraday Soc.*, 1948, **44**, 159, **171**, 243.
[2] Barrera i Costa, *Ann. Chim.* (*France*), 1949, **4**, 84.
[3] Cauquil and Barrera, *Bull. Soc. chim. France*, 1949, **16**, 689, 837.
[4] Burton and Praill, *J.*, (*a*) 1950, 2034; (*b*) 1951, 522, 529; (*c*) 1953, 827.
[5] Burton, *J. Roy. Inst. Chem.*, 1954, 242.
[6] Braun and Rath, *Ber.*, 1927, **60**, 1182.

presence of the cation. The results for $n = 2$ are in a sense complementary to those of Rothstein [7] who found that increasing proportions of open-chain ketone are produced when β-phenylpropionyl chloride is treated with aluminium chloride in the presence of increasingly active aromatic compounds; formation of diketone does not occur, of course, under his experimental conditions.

When $n = 3$, the ease of cyclisation, as expected, is much greater than that of substitution in the α-methylene group, so that no diketone is produced; in fact it is so great that some cyclisation (0·05 mole) occurs even in competitive reaction with anisole, 0·74 mole of open-chain ketone being produced at the same time.

The phenylacetyl cation has also been investigated for comparison and was found to be the most active of the series. Toluene was attacked at 0° to form *p*-phenylacetyltoluene in 59% yield, whilst with anisole in nitromethane the cation gave *p*-phenylacetylanisole (94%).

The formation of the diketones may, as expected, be carried out in two successive stages. Indan-1-one (1 mole) in nitromethane yields, on treatment with β-phenylpropionyl perchlorate (1 mole), in the very short time of ten minutes, 0·26 mole of the diketone. Indan-1-one (0·50 mole) and 0·20 mole of β-phenylpropionic acid may also be recovered from the reaction product together with a quantity of intractable tar (which is formed to some extent in most of the reactions described and may arise by self-condensation of the cyclic ketones under the influence of the perchloric acid formed in all these acylations).

This reaction may also account for the diminution in yield noticed when the reaction mixtures were left for longer times; *e.g.*, the yield of benzosuberone decreased from 10% to 1·3% when the reaction time was increased from 3 to 18 hours.

These experiments led us to attempt the acetylation of some cyclic ketones, generating the acetylium perchlorate by both the previous methods used, *i.e.*, by the use of equimolecular quantities of silver perchlorate and acetyl chloride, method (A), which was more efficient than acetic anhydride–perchloric acid mixtures, method (B). Indan-1-one, *cyclo*pentanone, 1-tetralone, and *cyclo*hexanone gave the 2-acetyl derivatives in yields of 88, 52, 30, and 13% respectively by method A, and 14, 9, 7, and 5% respectively by method B. The low yields with *cyclo*hexanone are due to its proneness to self-condensation. *cyclo*Hexylidene*cyclo*hexanone may be obtained in 25—30% yields by treatment of *cyclo*hexanone with a few drops of aqueous 70% perchloric acid in nitromethane, together with further condensed products, whilst from anhydrous systems containing acetic anhydride and perchloric acid dodecahydrotriphenylene has been isolated in 5% yield from the viscous residues.

Barrera i Costa [2] in his discussion of the mechanism of the cyclisation of arylaliphatic acids attributed the power of silver perchlorate to cyclise suitably constituted acyl halides solely to its ability to act in a manner similar to stannic chloride, anhydrous zinc chloride, etc., *i.e.*, as a Lewis acid.

To prove that it was the "Lewis acid" nature of the silver perchlorate that was causing cyclisation and not just its power to generate by metathesis a silver halide and an acyl perchlorate, $R{\cdot}CO{\cdot}ClO_4$, which incidentally he regarded as a mixed anhydride cyclising either spontaneously or under the influence of more silver perchlorate, he carried out experiments using methyl cyanide as solvent in place of benzene or toluene.

He suggested that methyl cyanide, acting as a base according to the Lewis theory, would neutralise the Lewis acid nature of the silver perchlorate and no cyclisation would result; he found this to be so. We cannot agree with this view and we have therefore investigated the cyclisation in methyl cyanide, of the above series of phenylalkanoyl perchlorates.

We have found that acylation still takes place but only where a highly nucleophilic centre exists, *i.e.*, when $n = 3$ (60% of 1-tetralone formed) or when anisole is present

[7] Rothstein, *J.*, 1951, 1459.

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(86% of *p*-β-phenylpropionylanisole formed from the perchlorate; $n = 2$). In other cases most of the original acid chloride is recovered as the acid, *e.g.*, with the perchlorate, $n = 2$ or $n = 4$, alone, 79 and 91%, respectively, of the corresponding acids were isolated, together with small amounts of products such as *N*-acetyl-β-phenylpropionamide (2%) which had arisen by interaction with the solvent. The formation of these products will be discussed more fully below.

Similar results were obtained when phenyl or benzyl cyanide was used as the solvent. In the former, the perchlorate, $n = 2$, reacted with anisole to give the straight-chain ketone in 70% yield, and, in the latter, the perchlorate, $n = 3$, gave 1-tetralone in 82% yield.

Our interpretation of these partly successful acylations in cyanide solutions is that the metathesis occurs as before but that the perchlorate is now solvated, *e.g.*, $(MeCN)_n \cdots RCO^+ClO_4^-$. This solvation diminishes the electron demand of the perchlorate and hence its acylating activity.[8] Consequently, the reactions which occurred most readily in nitromethane have still taken place in methyl cyanide, etc., but with smaller yields, whilst those which occurred less readily in nitromethane have been completely inhibited, *e.g.*, the intramolecular acylation with β-phenylpropionyl perchlorate does not take place in any of the cyanides. But as acylation depends both on the electrophilic activity of one component and the nucleophilic activity of the other it should be possible for the lowered reactivity of the β-phenylpropionyl cation to be still sufficiently high for a reaction to occur with a more highly reactive nucleophile. This is so: anisole is acylated in good yields by the perchlorate, $n = 2$, in all three cyanides.

On filtration of the reaction mixture it was noticed that quantitative yields of silver chloride were not now obtained as had been the case when hydrocarbons or nitromethane was used as the solvent, but that the deficiency was made up on hydrolysis of the reaction product with water. The amount of the deficiency was, in the case of methyl or benzyl cyanide, approximately equivalent to the amount of organic acid recovered by alkaline extraction of the reaction product; with phenyl cyanide the deficiency was approximately equivalent to half of the acid recovered (see Table). (We must stress here that these results are from semiquantitative experiments designed to explore the general reactions of these perchlorates and whilst the usual precautions were taken to exclude moisture, etc., the rigorous conditions necessary in work of a "kinetic" standard were not employed.)

TABLE

Expt. no.	Solvent	Perchlorate $Ph\cdot[CH_2]_n\cdot CO\cdot ClO_4$	Reactant	AgCl on hydrol. (%)	Org. acid recovered (%)
a	MeCN	$n = 1$	—	93	91
b	,,	,, 2	—	76	79
c	,,	,, 2	—	68	67
d	,,	,, 3	—	19	18
e	,,	,, 4	—	82	91
f	,,	,, 2	Anisole	16	0
g	$Ph\cdot CH_2\cdot CN$	,, 1	—	53	62
h	,,	,, 2	—	49	53
i	,,	,, 3	—	2	3
j	PhCN	,, 1	—	36	78
k	,,	,, 2	—	37	77
l	,,	,, 2	Anisole	0	23

We attribute the non-appearance of all of the silver chloride and the correlation between the "silver chloride on hydrolysis" and the "recovered organic acid" to the formation of a soluble complex between the silver chloride and equivalent amounts of organic perchlorate in methyl and benzyl cyanide, and twice the equivalent in phenyl cyanide. Cyanide molecules must also be involved in the complexes. We obtained evidence for the formation of soluble complexes containing silver salts in the following experiments.

[8] Baddeley, *Quart. Rev.*, 1954, **4**, 369.

First, when a solution of phenylacetyl perchlorate in nitromethane was added to an equal volume of methyl cyanide containing a suspension of silver chloride and the mixture shaken, 19% of the silver chloride went into solution during 3½ hours at room temperature; when anhydrous perchloric acid was substituted for the phenylacetyl perchlorate, 17% went into solution in 3 hr. The effect of nitromethane in the latter experiment may be judged from the fact that only 58% of the theoretical amount of silver was obtained as silver chloride when equivalent amounts of hydrogen chloride and silver perchlorate each in methyl cyanide were mixed and left at room temperature for 21 hr. The presence of anisole did not upset the latter equilibrium greatly, whereas silver nitrate in place of the perchlorate gave rapid and quantitative yields of silver chloride. Silver chloride is not soluble in methyl cyanide alone.

The reactions in methyl and benzyl cyanides may be summarised thus:

$$R'CN\cdots AgClO_4 + RCl \longrightarrow R'CN\cdots R^+ClO_4^- + AgCl$$

$$R'CN\cdots R^+ClO_4^- + AgCl \xrightarrow{ArH} RAr + R'CNH\cdots AgCl^+ClO_4^-$$

$$RAr + AgCl + R'CN + HClO_4$$

$$[R'CNR\cdots AgCl]^+ClO_4^-$$

where R′ = Me or Ph·CH_2, and R = Ph·$[CH_2]_n$·CO or H, and ArH is an active benzene derivative. When $n = 3$, ArH may be considered to be contained in R.

The yields of *N*-substituted amides, referred to above, were always small, *e.g.*, 2% and 4% of *N*-acetyl- and *N*-benzoyl-propionamide were formed by the perchlorate ($n = 2$) in methyl and phenyl cyanide respectively. Generally, the reaction products from methyl cyanide solution were " cleaner " than those from the other cyanides; from the viscous gums formed in benzyl cyanide, phenylacetamide as well as acylated phenylacetamides were often isolated. The perchlorate ($n = 1$) gave rise to 7% each of phenylacetamide and diphenyldiacetylamine, whilst only 38% of the perchlorate was recovered as the acid, the rest being a viscous tar.

It seems probable that the small amounts of *N*-acylamides have been produced by the addition of the perchlorate to the solvent:

$$RCN + Ph\cdot[CH_2]_n\cdot CO^+ClO_4^- \longleftrightarrow (R\cdot C{:}\overset{+}{N}\cdot CO\cdot[CH_2]_n\cdot Ph)ClO_4^-$$

$$(R\cdot \overset{+}{C}{:}N\cdot CO\cdot[CH_2]_n\cdot Ph)ClO_4^-$$

Subsequent hydrolysis of the carbonium ion would give rise to the *N*-acylamide:

$$R\cdot \overset{+}{C}{:}N\cdot CO\cdot[CH_2]_n\cdot Ph + OH^- \longrightarrow R\cdot CO\cdot NH\cdot CO\cdot[CH_2]_n\cdot Ph$$

We cannot find any references in the literature concerning the addition of acyl cations to ·C:N, but additions of alkyl cations to cyanides have been described recently by several authors. Ritter *et al.*[9] have reported the addition of olefins and tertiary and secondary alcohols to a wide variety of cyanides, the last-named addendum in concentrated sulphuric acid and the first two in acetic acid with an equivalent of sulphuric acid present. The addition of triphenylmethyl nitrate to methyl cyanide has been substantiated,[10,11] whilst Kornblum and his co-workers [12] quoting the work of Taub,[13] report the addition of the

[9] See Plaut and Ritter, *J. Amer. Chem. Soc.*, 1951, **73**, 4076 for earlier references.
[10] Cheeseman, *Chem. and Ind.*, 1954, 281.
[11] Cristol and Leffler, *J. Amer. Chem. Soc.*, 1954, **76**, 4468.
[12] Kornblum, Smiley, Blackwood, and Iffland, *ibid.*, 1955, **77**, 6271.
[13] Taub, Ph.D. Thesis, Purdue, 1952.

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tert.-butyl cation to methyl cyanide. Cast and Stevens [14] described the addition of the diphenylmethyl cation (derived from the sulphate) to methyl cyanide.

It is interesting that the *N*-acylamide obtained by the formation of β-phenylpropionyl perchlorate in benzyl cyanide is diphenyldiacetylamine and not the asymmetrical *N*-acylamide. This has probably arisen from the further addition of $(R'\cdot\overset{+}{C}{:}N\cdot CO\cdot[CH_2]_2\cdot Ph)ClO_4^-$ across a molecule of the solvent:

$$(R'\cdot\overset{+}{C}{:}N\cdot CO\cdot[CH_2]_2\cdot Ph)ClO_4^- + R'CN \longrightarrow R'\cdot\overset{+}{C}{:}N\cdot C(R'){:}N\cdot CO\cdot[CH_2]_2Ph$$

hydrolysis of the product would give diphenyldiacetamide.

Particular care has been taken to use cyanides free from amides as these are readily acylated by the perchlorates.

Experimental

Materials.—Silver perchlorate [16] was dried as previously described. Nitromethane, anisole, toluene, *cyclo*pentanone, *cyclo*hexanone, and 1-tetralone were dried and redistilled. Acetic anhydride and perchloric acid (72%) were "AnalaR" reagents. Methyl, phenyl, and benzyl cyanide were repeatedly distilled from phosphoric oxide.

Procedure.—The general procedure used in experiments involving silver perchlorate was to add, at a controlled temperature, a solution of the acid chloride in the appropriate solvent to a solution of silver perchlorate in a mixture of the same solvent and the reactant, if any. After a variable period the silver chloride was filtered off, the filtrate being allowed to fall on crushed ice. The silver chloride was then washed with water and ether. Any further silver chloride which separated in the combined filtrate and washings was subsequently filtered off before these were washed free from acids with sodium hydrogen carbonate solution. Any acid derived from unchanged organic perchlorate was then recovered by extraction of the acidified washings with ether. It was frequently identified by m. p. and mixed m. p. Treatment of the reaction product after removal of the dried (Na_2SO_4) solvents varied from experiment to experiment.

Reaction of β-Phenylpropionyl Perchlorate.—(a) *In nitromethane.* β-Phenylpropionyl chloride (0·05 mole) in nitromethane (30 c.c.) was added during 10 min. to a cold (0—2°) solution of silver perchlorate in nitromethane (70 c.c.). After a further 50 min. the reaction was stopped. β-Phenylpropionic acid (0·7 g.) was recovered and the product (6·2 g.) was treated with a saturated solution of copper acetate in ethyl alcohol until no more of the copper salt (m. p. after recrystallisation from benzene, 218°) of the diketone was precipitated. The *2-β-phenylpropionylindan-1-one* (3·0 g.), m. p. 64°, was obtained by treatment of the salt with 2N-sulphuric acid. Recrystallisations from ethyl alcohol raised the m. p. of the white plates to 71° (Found: C, 81·6; H, 6·5. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%). The *dioxime*, recrystallised from ethyl alcohol, had m. p. 187° (decomp.) (Found: C, 72·8; H, 6·2; N, 9·7. $C_{18}H_{18}O_2N_2$ requires C, 73·4; H, 6·1; N, 9·5%).

Steam-distillation of the residue gave indan-1-one, m. p. 39°, identified by the m. p. and mixed m. p. of the 2 : 4-dinitrophenylhydrazone (254—255°).

(b) *In toluene.* β-Phenylpropionyl chloride (0·05 mole) in toluene (30 c.c.) was added during 90 min. to a solution of silver perchlorate (0·05 mole) in toluene (70 c.c.) at 24°. After 3 hr. the reaction was stopped. β-Phenylpropionic acid (1·0 g.) was recovered. The reaction product (9·2 g.) gave, on crystallisation from ethyl alcohol, *p*-β-phenylpropionyltoluene (4·3 g.), m. p. 69°; distillation of the residue at 0·7 mm. gave (i) 0·6 g., b. p. 80—86°, (ii) 1·8 g., b. p. 150—170°, mainly 160—162°. Fraction (i) was indan-1-one, identified as before, and (ii) was the tolyl ketone, m. p. 69° (Burton and Ingold [15] give m. p. 70—71°).

(c) *With toluene in nitromethane.* β-Phenylpropionyl chloride (0·05 mole) in nitromethane (30 c.c.) was added in 20 min. to a cold (0—2°) solution of silver perchlorate in toluene (0·1 mole) and nitromethane (60 c.c.), and the reaction allowed to proceed for 3 hr. β-Phenylpropionic acid (0·6 g.) was recovered. The product was distilled at 1·5 mm., yielding fractions (i) 1·3 g., b. p. 88—94°, (ii) 0·7 g., b. p. 106—162°, (iii) 4·5 g., b. p. 162—174° (mainly 168°),

[14] Cast and Stevens, *J.*, 1953, 4180.
[15] Burton and Ingold, *J.*, 1928, 916.

and (iv) residue, 1·7 g. Fraction (ii) was a mixture of fraction (i) which was indan-1-one, identified as before, and fraction (iii) which was the tolyl ketone, m. p. 69—70°. The residue gave a copper salt, m. p. and mixed m. p. with that obtained in (a), 217°.

(d) *With anisole in nitromethane.* Repetition of expt. (c) with anisole (0·05 mole) in place of toluene and at 25° during 45 min. gave a crystalline product (10·7 g.), m. p. 95—96°. Rothstein [7] gives the m. p. of *p*-β-phenylpropionylanisole as 102°.

Reactions of δ-Phenylvaleryl Perchlorate.—(a) *In nitromethane.* δ-Phenylvaleryl chloride (0·05 mole) in nitromethane (30 c.c.) was added in 25 min. to a cold (0°) solution of silver perchlorate (0·05 mole) in nitromethane (70 c.c.), and reaction allowed to proceed at 2° for 3 hr.: δ-phenylvaleric acid (1·6 g.) was recovered. The product was separated into parts soluble (2·2 g.) and insoluble (3·5 g.) in sodium hydroxide. The latter part yielded on treatment with 2 : 4-dinitrophenylhydrazone (4·5 g.) in ethanolic sulphuric acid a tacky derivative (5·5 g.), which on recrystallisation from ethyl acetate gave 2 : 3-benzosuberone 2 : 4-dinitrophenylhydrazone (1·9 g.), m. p. and mixed m. p. 204°. The other portion, which gave an intense violet colour with aqueous-alcoholic ferric chloride, yielded a viscous copper salt (4·3 g.) when treated as described in (a) above.

In a second experiment (18 hr. at 3°) only 0·22 g. of the 2 : 4-dinitrophenylhydrazone of 2 : 3-benzosuberone was isolated.

(b) *In toluene.* δ-Phenylvaleryl chloride (0·025 mole) in toluene (20 c.c.) was added during 15 min. to a solution of silver perchlorate (0·025 mole) in toluene (40 c.c.) at 2°. The reaction was stopped after 3½ hr.: δ-phenylvaleric acid (3·2 g.) was recovered and the product, a dark oil (2·0 g.), yielded by the usual procedure *p*-δ-phenylvaleryltoluene 2 : 4-dinitrophenylhydrazone (220 mg.), m. p. and mixed m. p. 156°.

(c) *With anisole in nitromethane.* δ-Phenylvaleryl chloride (0·025 mole) in nitromethane (20 c.c.) was added in 10 min. to a cold (2°) solution of silver perchlorate (0·025 mole) in anisole (3·0 g.) and nitromethane (40 c.c.); the reaction was stopped after 30 min. The product (6·7 g.) crystallised as plates from ethyl alcohol; the m. p. 38° was increased to 39° by recrystallisation of the p-δ-*phenylvalerylanisole* twice more from ethyl alcohol (Found: C, 80·0; H, 7·3. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·4%). A 2 : 4-*dinitrophenylhydrazone* crystallised as bright red prisms, m. p. 140°, from ethyl acetate, and an *oxime* was obtained as thick rods, m. p. 85°, from ethyl alcohol–light petroleum (Found: C, 75·7; H, 7·6; N, 5·1. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·4; N, 4·9%).

Reactions of γ-Phenylbutyryl Perchlorate.—(a) *In nitromethane.* γ-Phenylbutyryl chloride (0·05 mole) in nitromethane (20 c.c.) was added at 24° in 20 min. to a solution of silver perchlorate (0·05 mole) in nitromethane (70 c.c.). After 30 min. more the reaction was stopped: γ-phenylbutyric acid (0·5 g.) was recovered. The product was distilled at 1 mm., yielding the fractions: (i) 4·8 g., b. p. 92—95°, (ii) 0·5 g., b. p. 96—116°, (iii) 0·4 g., b. p. 116—180°, and (iv) 1 g. of viscous residue. Fractions (i) and (ii) were 1-tetralone, identified by the m. p. and mixed m. p. 256° of the 2 : 4-dinitrophenylhydrazone. Fraction (iii) also contained tetralone, but like the residue, did not give a colour with aqueous-alcoholic ferric chloride.

(b) *With anisole in nitromethane.* γ-Phenylbutyryl chloride (0·05 mole) in nitromethane (25 c.c.) was added in 30 min. to a solution of silver perchlorate (0·05 mole) in anisole (5·8 g.) and nitromethane (70 c.c.) at 23°. The reaction was stopped after 1 hr. and γ-phenylbutyric acid (0·5 g.) was recovered. The product crystallised from ethyl alcohol, yielding p-γ-*phenylbutyrylanisole* (4·6 g.), m. p. 56°. Recrystallisation from ethyl alcohol raised the m. p. of the plates to 59°. Fractionation of the remainder of the product (6·3 g.) gave (i) 0·4 g., b. p. 120°/2—3 mm., (ii) 4·8 g., b. p. 226—232°/2 mm., and (iii) 1·1 g. of residue. Fraction (i) was 1-tetralone, identified as above, and fraction (ii) which crystallised from ethyl alcohol had m. p. 56—57°, and was identical with the *p*-γ-phenylbutyrylanisole which crystallised from the reaction product (Found: C, 80·2; H, 7·5. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

Reactions of Phenylacetyl Perchlorate.—(a) *In toluene.* Phenylacetyl chloride (0·05 mole) in toluene (25 c.c.) was added in 20 min. to a solution of silver perchlorate (0·05 mole) in toluene (70 c.c.) at −2°. After 3 hr. at +7° the reaction was stopped. After the recovery of phenylacetic acid (1·3 g.), the semi-solid product (8·7 g.) crystallised from alcohol to yield *p*-phenylacetyltoluene (5·0 g.), m. p. 108°; a further 1·2 g., m. p. 104°, were obtained on concentration of the mother-liquors.

(b) *With anisole in nitromethane.* Phenylacetyl chloride (0·05 mole) in nitromethane (20 c.c.) was added in 15 min. to a solution of silver perchlorate (0·05 mole) in anisole (6 g.) and

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nitromethane (70 c.c.) at −2°. After an hour at +2° the reaction was stopped, and phenylacetic acid (0·4 g.) was recovered. The product, a solid mass (11·3 g.), gave, on crystallisation from ethyl alcohol–light petroleum (b. p. 60—80°), *p*-phenylacetylanisole (9·5 g.), m. p. 77°; a further 1·1 g., m. p. 75—76°, were obtained from the mother-liquor.

Reaction of β-Phenylpropionyl Perchlorate with Indan-1-one.—β-Phenylpropionyl chloride (0·05 mole) in nitromethane (30 c.c.) was added in 2 min. to a solution of silver perchlorate (0·05 mole) and indan-1-one (0·05 mole) in nitromethane (70 c.c.) at 0°. The reaction was stopped after 10 min. The product (10·9 g.), after removal of β-phenylpropionic acid (1·5 g.), was fractionally distilled, giving (i) 1·2 g., b. p. 130°/2 mm., (ii) 2·1 g., b. p. 130—140°/2 mm., (iii) 3·5 g., b. p. 226—232°/2 mm., (iv) 4·0 g., of a viscous mixture. Fractions (i) and (ii) were indan-1-one, and fraction (iii) crystallised to give pale yellow plates of 2-β-phenylpropionylindan-1-one, m. p. 68—69°. Both products were identified as above.

Acetylation of Some Cyclic Ketones.—(a) *Using silver perchlorate and acetyl chloride.* (i) Indan-1-one. Indan-1-one (0·05 mole) and silver perchlorate (0·05 mole) were dissolved in nitromethane (70 c.c.) and treated with acetyl chloride (0·05 mole) in nitromethane (30 c.c.) during 25 min. at 18°. After a further hour the silver chloride was filtered off from the intensely red solution which was allowed to fall on crushed ice. The silver chloride was washed with ether and water. Adding the ether washings to the filtrate gave an orange solid (0·4 g.), which exploded quietly on being heated. This was filtered off and the filtrate washed until alkaline with sodium hydrogen carbonate solution. The dried (Na_2SO_4) solution yielded, after the removal of the solvents, 2-acetylindan-1-one (7·7 g.), which after recrystallisation from methyl alcohol melted at 77°. A *dioxime* crystallised as fine white needles (from ethyl acetate), m. p. 175° (Found: C, 64·6; H, 6·0. $C_{11}H_{12}O_2N_2$ requires C, 64·7; H, 5·9%).

(ii) *cyclo*Pentanone. Acetyl chloride (0·05 mole) in nitromethane (20 c.c.) was added during 15 min. at 4—8° to a solution of silver perchlorate in nitromethane (70 c.c.) and *cyclo*pentanone (5 g.). After a further 90 min. at 5° the silver chloride was filtered off from the orange solution, and the filtrate allowed to fall on crushed ice. The product treated in the usual way gave, on distillation at 18 mm., 3·5 g. of diketonic material, b. p. 88°. A viscous black residue (4·7 g.) remained. The *disemicarbazone* crystallised as white needles (from ethanol), m. p. 215° (Found: C, 45·1; H, 6·6; N, 35·6. $C_9H_{16}O_2N_6$ requires C, 45·0; H, 6·7; N, 35·0%).

(iii) 1-Tetralone. Acetyl chloride (0·05 mole) in nitromethane (70 c.c.) was added during 15 min. at 0° to a solution of silver perchlorate (0·05 mole) in nitromethane (70 c.c.) and 1-tetralone (8·0 g.). The silver chloride was filtered off from the fluorescent solution after a further hour. The product obtained in the usual way was dissolved in ether and separated into sodium hydroxide-soluble and -insoluble parts. The former (2·8 g.) was diketonic and yielded a *semicarbazone* as fine white needles, m. p. 179° (Found: C, 62·9; H, 5·9; N, 18·0. $C_{13}H_{15}O_2N_3$ requires C, 63·6; H, 6·1; N, 17·1%). Attempts to make an oxime or dioxime gave an *oxazole* as yellow prisms, m. p. 59° (Found: C, 77·0; H, 5·8; N, 7·6. $C_{13}H_{11}ON$ requires C, 77·8; H, 5·9; N, 7·6%). From the sodium hydroxide-insoluble part (5·6 g.) 1-tetralone (4·8 g.), b. p. 150—160°/2 mm., 256—257°/758 mm., was recovered.

(iv) *cyclo*Hexanone. Acetyl chloride (0·05 mole) in nitromethane (20 c.c.) was added in 25 min. at 6° to a solution of silver perchlorate (0·05 mole) and *cyclo*hexanone (6·0 g.). After a further 3½ hr. the mixture was treated as above. The sodium hydroxide-soluble part (3·1 g.) gave on distillation 2-acetyl*cyclo*hexanone (0·9 g.), b. p. 102—111°/2 mm., identified as the semicarbazone, m. p. 161°.

(b) *Using acetic anhydride and perchloric acid.* (i) Indan-1-one. Indan-1-one (0·05 mole) in acetic anhydride (13 g.) was treated with 70% perchloric acid (0·0125 mole) and the reaction allowed to proceed at 15° for 90 min. The addition of water and ether caused the separation of an unstable orange perchlorate (0·98 g.). The sodium hydroxide-soluble part of the product crystallised as off-white needles (1·2 g.), m. p. 71°, mixed m. p. with 2-acetylindan-1-one, 74°. Recrystallisation from methyl alcohol raised the m. p. to 77°.

(ii) *cyclo*Pentanone. *cyclo*Pentanone (0·10 mole) in acetic anhydride (20 g.) was treated with a solution of 70% perchloric acid (0·025 mole) in nitromethane (20 c.c.) in 10 min. at 20°. The reaction was allowed to proceed for a further 2 hr. at 18° before the solution was poured into water and ether. The sodium hydroxide-soluble part of the product (2·1 g.) gave on distillation, 1·1 g. of material, b. p. 102—104°/33 mm., which gave a disemicarbazone identical with that previously obtained.

(iii) 1-Tetralone. 1-Tetralone (0·10 mole) in acetic anhydride (26 g.) and nitromethane

(40 c.c.) was treated with 70% perchloric acid (0·025 mole) in nitromethane (20 c.c.) at 5° during 5 min. The reaction was stopped after a further 3½ hr. at 5° and the mixture worked up as above to give 2-acetyl-1-tetralone (1·3 g.). 1-Tetralone (12 g.) was recovered.

(iv) *cyclo*Hexanone. *cyclo*Hexanone (0·20 mole) in acetic anhydride (40 g.) and nitromethane (15 c.c.) was treated at 2° during 30 min. with 70% perchloric acid (0·05 mole) in nitromethane (25 c.c.). After 3 hr. at 22—24° the red solution was poured into water and ether and worked up as above. 2-Acetyl*cyclo*hexanone (1·3 g.) was distilled from the sodium hydroxide-soluble part. It had b. p. 108—110°/16 mm. The sodium hydroxide-insoluble part contained unchanged *cyclo*hexanone (8 g.) and other products of b. p. >182°/16 mm. Dodecahydrotriphenylene (0·8 g.), m. p. 227°, crystallised from the residue.

Treatment of cyclo*Hexanone with* 70% *Perchloric Acid.*—*cyclo*Hexanone (0·20 mole) was treated with 70% perchloric acid (0·05 mole) at 18°. The reaction was stopped after 30 min. by addition of water and ether. The ethereal layer, washed free from acid, gave on distillation unchanged *cyclo*hexanone and 2-*cyclo*hexylidene*cyclo*hexanone (5·1 g.), b. p. 144—146°/18 mm. A semicarbazone, m. p. 178°, was prepared.

Reactions of the Perchlorates Alone in Methyl Cyanides.—(a) *γ-Phenylbutyryl perchlorate.* γ-Phenylbutyryl chloride (0·05 mole) in methyl cyanide (20 c.c.) was added during 15 min. to a solution of silver perchlorate (0·05 mole) in methyl cyanide (70 c.c.) at 6°. The reaction was stopped after a further 3½ hr., the insoluble silver chloride (5·8 g.) was collected and the filtrate allowed to fall on crushed ice. More silver chloride precipitated by this treatment was then collected. The product (7·2 g.), an orange oil, gave, after the removal from it of γ-phenylbutyric acid, 1-tetralone (4·5 g.), b. p. 104—111°/2—3 mm., identified as before.

(b) *δ-Phenylvaleryl perchlorate.* δ-Phenylvaleryl chloride was used in the place of the γ-phenylbutyryl chloride in an experiment similar to the above; δ-phenylvaleric acid (7·9 g.) was recovered from the product by extraction with sodium carbonate solution. Treatment of the remainder (1·8 g.) with aqueous ethanol resulted in the separation of δ-phenylvaleramide (0·3 g.), identified by the m. p. and mixed m. p. 107°, with an authentic sample of m. p. 108°.

(c) *β-Phenylpropionyl perchlorate.* β-Phenylpropionyl chloride, when treated as above, gave, after the removal of β-phenylpropionic acid (6·0 g.), a brown oil (2·6 g.) which on extraction with hot water gave *N*-acetyl-β-phenylpropionamide (190 mg.), m. p. and mixed m. p. 107°.

Reactions of the Perchlorates Alone in Phenyl Cyanide.—(a) *β-Phenylpropionyl perchlorate.* β-Phenylpropionyl chloride (0·05 mole) was added during 15 min. at 0° to a solution of silver perchlorate (0·05 mole) in phenyl cyanide (70 c.c.). After 3½ hr. the mixture was worked up in the usual way, to give β-phenylpropionic acid (5·4 g.) and a brown oil (3·1 g.) which partially crystallised, to give *N*-benzoyl-β-phenylpropionamide (460 mg.), m. p. 105° (Johnson and Chernoff [16] give the m. p. as 104—105°) (Found: C, 75·5; H, 6·2; N, 5·3. Calc. for $C_{16}H_{15}O_2N$: C, 75·9; H, 5·9; N, 5·5%).

(b) *Phenylacetyl perchlorate.* Phenylacetyl chloride (0·05 mole) was added during 10 min. at 0° to silver perchlorate (0·05 mole) in phenyl cyanide (60 c.c.). After 4 hr. the reaction was stopped and the mixture treated in the usual way. The phenyl cyanide was then removed in steam, leaving a brown oil (4·3 g.) which partially crystallised, to give *N*-benzoylphenylacetamide (260 mg.), m. p. and mixed m. p. 135°. The authentic sample of *N*-benzoylphenylacetamide was made by an analogous method to that described by Johnson and Chernoff [16] for the preparation of *N*-benzoylphenylpropionamide. Wheeler, Johnson, and MacFarland [17] give m. p. 129—130°.

Reactions of the Perchlorates Alone in Benzyl Cyanide.—(a) *Phenylacetyl perchlorate.* Phenylacetyl chloride (0·05 mole) in benzyl cyanide (20 c.c.) was added at 0° during 15 min. to a solution of silver perchlorate (0·05 mole) in benzyl cyanide (50 c.c.). After 1½ hr. more the reaction was stopped. Phenylacetic acid (2·6 g.) was recovered, and the benzyl cyanide removed by steam-distillation. The crude product (6·8 g.) partially crystallised from ethanol, to give yellowish plates (1·1 g.), m. p. 184°, which, recrystallised from ethanol, had m. p. 190° and mixed m. p. 192° with diphenylacetamide (m. p. 194°) made by the method of Colby and Dodge.[18] Hot-water extracts of the residue gave brown plates (0·79 g.), m. p. *ca.* 120°. Recrystallisation of these from benzene gave phenylacetamide (0·50 g.), m. p. 156°.

(b) *β-Phenylpropionyl perchlorate.* β-Phenylpropionyl chloride (0·05 mole) in benzyl

[16] Johnson and Chernoff, *J. Amer. Chem. Soc.*, 1911, **33**, 520.
[17] Wheeler, Johnson, and MacFarland, *ibid.*, 1903, **25**, 795.
[18] Colby and Dodge, *Amer. Chem. J.*, 1891, **13**, 3.

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cyanide (20 c.c.) was added in 10 min. at 2° to a solution of silver perchlorate (0·05 mole) in benzyl cyanide (70 c.c.). After 2½ hr. the reaction was stopped. Diphenyldiacetylamine (0·55 g.) and phenylacetamide (140 mg.) were obtained and identified as in the preceding experiment. The crude product (5·4 g.) did not contain any phenylpropionamide.

(c) *γ-Phenylbutyryl perchlorate.* γ-Phenylbutyryl chloride (0·05 mole) in benzyl cyanide (20 c.c.) was added to a cold (4°) solution of silver perchlorate (0·05 mole) in benzyl cyanide during 10 min. After 2½ hr. at 5° the reaction was stopped, and phenylbutyric acid (0·3 g.) was recovered. The amount of 1-tetralone in the steam-volatile part of the product was determined by treating part of it with Brady's reagent. A one-tenth part yielded 1·33 g. of 1-tetralone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 256°. The non-steam-volatile part (1·1 g.) partially crystallised, to give phenylacetamide (48 mg.), m. p. and mixed m. p. 155—157°.

Reactions with Anisole in Alkyl Cyanide Solutions.—(a) *In methyl cyanide.* β-Phenylpropionyl chloride (0·025 mole) in methyl cyanide (15 c.c.) was added in 15 min. to a solution of silver perchlorate (0·025 mole) in methyl cyanide (35 c.c.) at 20°. The reaction was stopped after 35 min. more and a trace of the acid recovered. The product, a pasty mass (7·2 g.), gave *p*-β-phenylpropionylanisole (5·4 g.), identified as before.

(b) *In phenyl cyanide.* In an experiment similar to the above but with phenyl cyanide in place of methyl cyanide, β-phenylpropionic acid (0·9 g.) was recovered and the yield of *p*-β-phenylpropionylanisole was reduced to 4·2 g.

Solubility of Silver Chloride in the Presence of Alkyl Cyanides and Some Perchlorate.—(a) *In the presence of methyl cyanide and phenylacetyl perchlorate.* A solution of phenylacetyl perchlorate was made by mixing equimolecular amounts of phenylacetyl chloride (0·025 mole) in nitromethane (5 c.c.) and silver perchlorate in nitromethane (40 c.c.). The silver chloride was filtered off and washed with nitromethane (5 c.c.), and the washings were added to the solution. Silver chloride (6·195 g.) was then added, followed by methyl cyanide (50 c.c.), and the mixture shaken for 3½ hr. at room temperature. The silver chloride was then filtered off; it amounted to only 5·032 g.

(b) *In the presence of methyl cyanide and anhydrous perchloric acid.* In an experiment similar to the above but with hydrogen chloride in the place of the acid chloride, only 2·087 g. of silver chloride were filtered off out of a total of 2·518 g. after 3½ hr. at room temperature.

p-δ-*Phenylvaleryltoluene.*—Aluminium chloride (2 g.) was added to a cooled (ice-salt) mixture of δ-phenylvaleryl chloride (4 g.), toluene (20 c.c.), and light petroleum (b. p. 60—80°; 50 c.c.); the mixture was then allowed to warm to room temperature and heated on a water-bath until the evolution of hydrogen chloride had ceased. After 4 hr. more at room temperature it was worked up in the usual way. Distillation of the product gave the *ketone* (2·4 g.), b. p. 228—230°/2 mm. A 2 : 4-*dinitrophenylhydrazone* crystallised as orange needles (from ethyl acetate), m. p. 156° (Found: C, 66·1; H, 5·6; N, 13·3. $C_{24}H_{24}O_4N_4$ requires C, 66·6; H, 5·5; N, 13·0%).

N-*Acetyl*-β-*phenylpropionamide.*—β-Phenylpropionyl chloride (8·5 g.) was added to acetamide (3·0 g.) dissolved in pyridine (30 c.c.), and the solution heated on a water-bath for 6 hr. It was then poured into water and ether. The ether-soluble part yielded a pasty mass on removal of the solvents, and this on subsequent recrystallisations from light petroleum gave the *N-acylamide*, m. p. 105° (Found: C, 68·9; H, 6·8; N, 7·0. $C_{11}H_{13}O_2N$ requires C, 69·1; H, 6·8; N, 7·3%).

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QUEEN ELIZABETH COLLEGE (UNIVERSITY OF LONDON),
LONDON, W.8.

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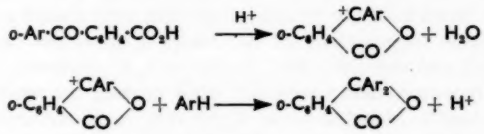
327. *Acylation and Allied Reactions Catalysed by Strong Acids. Part XVII.* Perchloric Acid as a Catalyst for the Formation of Phthalides from o-Aroylbenzoic Acids.*

By H. Burton and D. A. Munday.

In view of reports that silver perchlorate can catalyse the formation of phthalides from *o*-benzoylbenzoic acid and an aromatic component, this use has been investigated. Both anhydrous and 72% perchloric acid are effective, even at room temperature. Related experiments with phthaloyl chloride and succinyl chloride and silver perchlorate in, *e.g.*, anisole are described.

Cauquil, Barrera, and Barrera [1,2,3] recently described the production of phthalides from *o*-benzoylbenzoic acid and a suitable aromatic compound using silver perchlorate as a catalyst. However, in view of previous reports [4] of the alleged catalytic activity of silver perchlorate, and the fact that Cauquil, Barrera, and Barrera state [3] that they made no attempt to remove perchloric acid from their silver perchlorate, in which it is a common contaminant, we decided to see whether the true catalyst might not be perchloric acid, in which case the reactions would undoubtedly proceed as follows:



The regeneration of the proton in the second stage would account for the activity of the perchloric acid as a catalyst.

As was reported briefly,[5] we have found that *o*-benzoylbenzoic acid (1 mole) when refluxed for 4 hr. in *m*-xylene with anhydrous perchloric acid (0·004 mole) in acetic acid gave 3-phenyl-3-(2 : 4-dimethylphenyl)phthalide in 64% yield. Cauquil and her collaborators obtained *ca.* 50% of the phthalide using *two* molecules of silver perchlorate per molecule of acid and refluxing the solution for 7 hr. When we performed an experiment similar to the latter but with equimolecular quantities of acid and silver perchlorate we obtained only 6·8% of phthalide after 4 hr. The silver perchlorate which we used had been dried by our usual method,[6] *i.e.*, as a fine powder in a vacuum-desiccator containing both phosphoric oxide and potassium hydroxide pellets. This procedure has been shown to remove most, but not always all, of the perchloric acid from the perchlorate. However, the discrepancy in the yields of phthalide obtained by the French workers and ourselves using silver perchlorate, coupled with our demonstration that under similar conditions perchloric acid is, on a molecular basis, roughly two-thousand times more efficient than silver perchlorate, strongly suggests that perchloric acid is the true catalyst. We obtained further support for this view by treating the silver perchlorate with a little silver acetate before addition of the keto-acid. In one experiment the yield of phthalide was reduced to 0·7% after a total of 14 hr. when the silver perchlorate had been first refluxed with silver acetate (0·002 mole) for 2 hr.

At room temperature the reaction with *m*-xylene proceeds slowly, only 1·3% of 3-phenyl-3-(2 : 4-dimethylphenyl)phthalide being produced in 14 days from similar amounts

* Part XVI, preceding paper.

[1] Cauquil, Barrera, and Barrera, *Bull. Soc. chim. France*, 1951, **18**, 173.
[2] *Idem, ibid.*, 1952, **19**, 248.
[3] *Idem, ibid.*, 1955, **22**, 550.
[4] Burton and Praill, *J.*, 1953, 837.
[5] Burton and Munday, *Chem. and Ind.*, 1956, 316.
[6] Burton and Praill, *J.*, 1950, 2034.

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of the acids as were used above; equivalent quantities of the keto-acid and anhydrous perchloric acid in nitromethane as solvent gave 5·6% after 2 hr. It is thus not surprising that when the reaction was allowed to proceed for short periods only we were able to isolate *o*-2 : 4-dimethylbenzoylbenzoic acid and *o*-2 : 4 : 6-trimethylbenzoylbenzoic acid from the product of the addition of silver perchlorate (1 mole) to phthaloyl chloride (1 mole) in the presence of *m*-xylene and mesitylene, respectively. Toluene does not give *o*-4-toluoylbenzoic acid in a similar reaction, but, contrary to Cauquil, Barrera, and Barrera's statement, does react with *o*-benzoylbenzoic acid to give 3-phenyl-3-*p*-tolylphthalide in 24% yield on refluxing for 14 hr. with the more efficient catalyst, perchloric acid (0·1 mole). Benzene is not reactive.

The reaction with anisole proceeds well; a quantitative yield of 3-phenyl-3-*p*-methoxyphenylphthalide was obtained when *o*-benzoylbenzoic acid (1 mole) was heated in an excess of anisole with 72% perchloric acid (0·05 mole) at 120—125° for 6 hr. Similar quantities of reactants in refluxing nitromethane (b. p. 101°) gave 58% of the phthalide after 4 hr.; at room temperature this relatively small amount of perchloric acid was not effective but an equimolecular quantity of anhydrous perchloric acid in nitromethane produced 60% of the phthalide after 2 hr.

These results with anisole are in sharp contrast to those of Cauquil and her co-workers, who although they found that anisole was the most reactive of the nucleophilic agents that they used, also found that the products were the most complex.

In their experiments they again used two moles of silver perchlorate to each mole of *o*-benzoylbenzoic acid and obtained, first, in the cold, a substance, b. p. 245°/3 mm., in addition to 95% of recovered acid; secondly, after heating the reactants on a water-bath for 5½ hr., they obtained a colourless syrup which they could not crystallise but which was presumably 3-phenyl-3-*p*-methoxyphenylphthalide for on reduction with zinc and sodium hydroxide it gave a good yield of 2-carboxy-4'-methoxytriphenylmethane; and, thirdly, after heating the reactants at 110—120° for 5½ hr., they obtained a high-boiling neutral fraction which on reduction as before gave a small amount of an ill-defined acid, m. p. 110—111°.

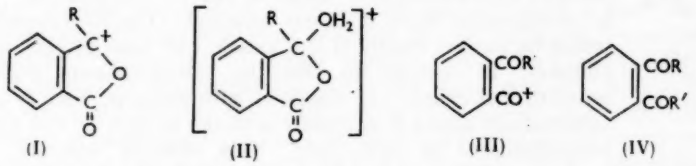
Phthaloyl chloride (1 mole) when treated with silver perchlorate (1 mole) in an excess of anisole gave no isolable amount of *o*-4-methoxybenzoylbenzoic acid, even when the reaction was carried out at −10° for 15 min., but gave instead moderate yields of di-*O*-methylphenolphthalein, 30% being obtained after 30 min. at 5°. This is not unexpected in view of the rapid reaction of *o*-anisoylbenzoic acid with anisole in the presence of an equivalent quantity of perchloric acid: we have obtained di-*O*-methylphenolphthalein in yields of 58 and 70% after 2 and 6 hr., respectively, at room temperature using anhydrous perchloric acid in acetic acid–nitromethane. Aqueous perchloric acid (72%) is only a little less effective, yields of the phthalide being 25—89% according to the conditions.

Some experiments have also been made in which succinyl chloride has been treated with silver perchlorate in the presence of active aromatic compounds. A high yield of an orange high-boiling oil was obtained from equimolecular quantities of the reagents in anisole–nitromethane. A similar reaction in *m*-xylene gave, as with phthaloyl chloride, a keto-acid; 2 : 4-dimethylbenzoylpropionic acid was obtained in 47% yield.

Addition of phthaloyl or succinyl chloride to two equivalents of silver perchlorate in *m*-xylene–nitromethane led to reduced yields of the keto-acids compared with those obtained when equimolecular amounts of the reagents were used. *o*-2 : 4-Dimethylbenzoylbenzoic and β-2 : 4-dimethylbenzoylpropionic acid were obtained in only 7 and 8% yield, respectively, from phthaloyl and succinyl chloride and *m*-xylene at room temperature. In each case the dibasic acid and its anhydride together with a little high-boiling material were the other products isolated.

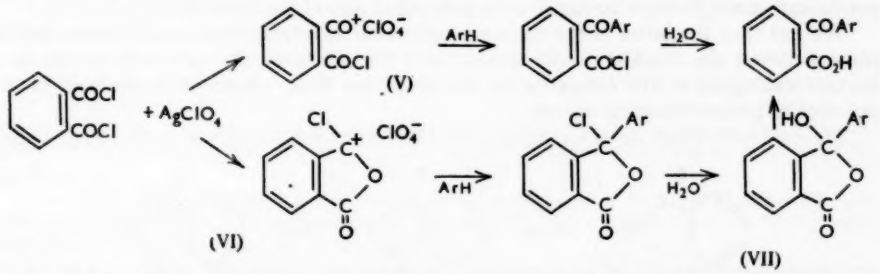
The high-boiling material obtained in experiments with succinyl chloride and *m*-xylene may have contained some γγ-bisdimethylphenyl-γ-butyrolactone, although our attempts to form this unknown lactone by heating under reflux β-2 : 4-dimethylbenzoylpropionic

acid and *m*-xylene in the presence of either a trace of 72% or an equivalent of anhydrous perchloric acid have failed. In each case the keto-acid was recovered almost quantitatively. The precursor of the phthalides produced in the acid-catalysed condensations of *o*-aroylbenzoic acids with active aromatic components is presumably a cyclic ion of the form (I), or possibly of the hydrated form (II). The well-known alternative mode of reaction of *o*-aroylbenzoic acids, *i.e.*, intramolecular cyclisation to form anthraquinone derivatives, *via* an intermediate keto-ion (III), was not observed in any of the above experiments. However, under more vigorous conditions, anthraquinone could be produced in small amounts, *e.g.*, in one experiment 8% was formed when *o*-benzoylbenzoic acid (1 mole) and anhydrous perchloric acid (2 moles) in acetic–nitromethane were heated under reflux for three hours in the absence of an active aromatic component. Diketones of the type (IV), which are stable in the presence of strong acids and do not rearrange to form phthalides would be produced readily by interaction of the keto-ion (III) with an aromatic component such as anisole. However, none of these diketones was found in our reaction products. Their absence, coupled with the demonstration that phthalide formation occurs much more readily than intramolecular acylation, indicates that the equilibrium which must exist



between the keto-ion (III) and the cyclic ion (I) lies almost completely in favour of (I), at room temperature and even at higher temperatures, *e.g.*, in boiling *m*-xylene.

Previously Luder and Zuffanti,[7] in view of Newman's [8] demonstration of the existence of the cyclic form of the ion, at low temperatures at least, had regarded its formation as an alternative and subsidiary reaction of the keto-ion produced from *o*-benzoylbenzoic acid and strong acids. What they did not realise and what our evidence shows clearly is that in the presence of strong acids the carbonium ion derived from *o*-benzoylbenzoic acid exists almost completely in the cyclic form to the exclusion of the keto-form, and that whilst the cyclic ion is a much more reactive entity than the keto-ion, in the absence of any nucleophilic component reaction occurs *via* the keto-form to give anthraquinone. The high yields of anthraquinone which can be obtained depend on the maintenance of the



equilibrium between the cyclic and the keto-ions and, whilst we have shown that the change " keto-ion to cyclic ion " must be very fast, the converse need not be true. We suggest that this last factor must be considered in assigning the rate-determining step in this rather remarkable intramolecular cyclisation.

[7] Luder and Zuffanti, (*a*) " The Electronic Theory of Acids and Bases," John Wiley and Sons, Inc., New York, 1946, p. 132; (*b*) *J. Amer. Chem. Soc.*, 1944, **66**, 524.
[8] Newman, *J. Amer. Chem. Soc.*, 1942, **64**, 2324.

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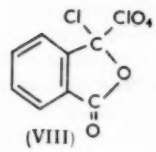
We are unable to decide conclusively on the present evidence as to the mode of formation of *o*-aroylbenzoic acids in the experiments in which silver perchlorate was added to an equimolecular amount of phthaloyl chloride in the presence of moderately active aromatic components such as *m*-xylene.

The simplest course is *via* the intermediate carbonium ion (V). However, there is the possibility that the reaction might occur *via* a cyclic ion (VI), giving a 3-aryl-3-chlorophthalide, which on hydrolysis would give the keto-acid by isomerisation of the unstable lactonic form.

Evidence in favour of the second reaction scheme includes the well-known isomerisation of phthaloyl chloride to the asymmetrical chloride in the presence of aluminium chloride [9] and other strong acids. However, with aluminium chloride the transformation is somewhat slower than that which must take place in our reactions. Of greater interest is the instability of the half-perchlorate derived from silver perchlorate and an equimolecular quantity of phthaloyl chloride in nitromethane solution in the absence of any nucleophilic component. We have found that when phthaloyl chloride in nitromethane is treated with silver perchlorate either at 0° or at room temperature the solution becomes yellow-green and oxides of chlorine are evolved. If anisole is subsequently added it is not attacked. Dimethylphenolphthalein would be formed readily if the anisole had been present during the addition. In contrast to this the half-perchlorate derived from terephthaloyl chloride is stable in nitromethane, and if anisole is subsequently added it is rapidly acylated to give 1 : 4-di-*p*-methoxybenzoylbenzene in 88% yield. This strongly suggests that the decomposition of the half-perchlorate derived from phthaloyl chloride occurs because of the mutual interaction of the two substituents *ortho* to one another. It seems very probable that a compound of the type (VIII) is formed and this eliminates chlorine dioxide leaving a diradical. Further, the absence of these decomposition products in experiments in which the organic perchlorate is formed *in situ* in, say, *m*-xylene suggests that cyclic compounds of the type (VIII) are not involved and that the acylation takes place through the non-cyclic carbonium ion (V).

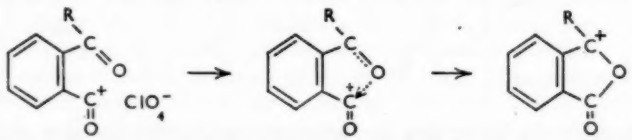


(VIII)

In the formation of di-*O*-methylphenolphthalein, the reaction presumably also begins in this way, rearrangement to the cyclic form occurring in either the intermediate *o*-aroylbenzoyl chloride or the *o*-aroylbenzoyl perchlorate. If cyclisation does occur by rearrangement of the acid chloride, it must be extremely rapid to allow metathesis of the lactide form to occur with the added silver perchlorate, whilst cyclisation of the *o*-aroylbenzoyl perchlorate must likewise be rapid to exclude diketones of the type (IV).

We feel that the latter is the most probable course, intramolecular association taking place between the doubly bound oxygen and the electronically deficient carbon in a manner analogous to the formation of the cyclic ion from *o*-benzoylbenzoic acid in the presence of proton-donating agents.

The ease with which the rearrangement to the cyclic form occurs was further emphasised

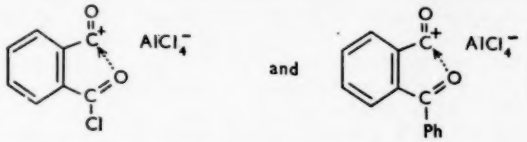


by the formation of 3-*p*-methoxyphenyl-3-phenylphthalide in almost quantitative yield when the metathetical reaction between silver perchlorate and *o*-benzoylbenzoyl chloride in nitromethane–anisole solution was allowed to proceed at −10° for 30 min.

Similar intermediates have been proposed by Baddeley [10] as being involved in the

[9] Ott, *Org. Synth.*, Coll. Vol. II, p. 528, John Wiley and Sons, Inc., New York, 1947.
[10] Baddeley, *Quart. Rev.*, 1954, **8**, 371.

isomerisation of phthaloyl chloride by aluminium chloride and in the aluminium chloride-catalysed production of phthalides from *o*-benzoylbenzoyl chloride and benzene.



The formation of the very reactive acetyl cation by the action of 72% perchloric acid on acetic anhydride ($Ac_2O + HClO_4 \longrightarrow Ac{\cdot}ClO_4 + AcOH$) has been thoroughly investigated.[11, 12]

We have now found that the analogous reaction does not occur with succinic or phthalic anhydride to an appreciable extent. Succinic anhydride, when added to 72% perchloric acid in anisole–nitromethane in the quantity calculated to dehydrate the perchloric acid and still be present in amount equivalent to the anhydrous perchloric acid formed, caused the solution to warm slowly and to become mauve. This colour darkened considerably in four days at room temperature. The product then contained a small amount (4% yield) of a substance whose properties indicated that it was γγ-bisdi-*p*-methoxyphenylbutyro-γ-lactone. The boiling of similar mixtures led to the formation of moderate amounts of intractable tars, whilst the use of anhydrous perchloric acid in acetic acid resulted in interaction between the acetic acid and the succinic anhydride with the consequent formation of succinic acid, which crystallised when the reaction mixture was kept at room temperature after it had been heated under reflux for 5 hr. The product in this experiment also was a viscous black tar.

Phthalic anhydride gave similar intractable tars.

These results are complementary to those of Flowers, Gillespie, and Wasif [13] who have recently contrasted the cryoscopic and conductometric behaviour of succinic and phthalic anhydride in sulphuric acid with the behaviour of acetic and benzoic anhydride under similar conditions. These authors found that, whereas the latter anhydrides are completely ionised in sulphuric acid solution, succinic acid is so probably only to the extent of 70%, whilst phthalic anhydride might well be 90% un-ionised.

Experimental

Materials.—Silver perchlorate was dried as previously described.[6]

Anhydrous perchloric acid in acetic acid was made by the careful addition of the calculated quantity of 72% perchloric acid to acetic anhydride at $<0°$.

Experiments with o-*Benzoylbenzoic Acid and* o-*Anisoylbenzoic Acid.*—In each case the keto-acid (0·025 mole) was dissolved in the appropriate solvent(s) and treated with silver perchlorate or perchloric acid as described in the text. After the prescribed interval the solution was poured into water, and the unchanged acid recovered with the aid of ether and sodium hydrogen carbonate or sodium carbonate solution. The neutral portion crystallised on removal of the solvents.

Di-*O*-methylphenolphthalein was identified by m. p. and mixed m. p.; 3-phenyl-3-(2 : 4-dimethylphenyl)phthalide,[3] 3-phenyl-3-*p*-tolylphthalide,[14] and 3-phenyl-3-*p*-methoxyphenylphthalide [15] were all as described in the literature.

Reaction of Silver Perchlorate with Phthaloyl Chloride.—(a) *In the presence of mesitylene.* Silver perchlorate (0·05 mole), dissolved in nitromethane (70 c.c.), was added during 15 min., at 5°, to a mixture of phthaloyl chloride (0·05 mole), mesitylene (0·11 mole), and nitromethane (20 c.c.). After 1·5 hr. the silver chloride was filtered off, the filtrate falling into cold water.

[11] Mackenzie and Winter, *Trans. Faraday Soc.*, 1948, **44**, 159, 171, 243.
[12] Burton and Praill, *J.*, 1950, 1203, 2034.
[13] Flowers, Gillespie, and Wasif, *J.*, 1956, 607.
[14] Limpricht, *Annalen*, 1898, **299**, 309.
[15] Meyer and Fischer, *Ber.*, 1911, **44**, 1953.

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Sodium carbonate extracts of the combined filtrate and washings (both water and ether) of the silver chloride yielded 5·1 g. of acid, m. p. 150—160°. Treatment of this with hot water (150 c.c.) removed phthalic acid and gave 2-(2 : 4 : 6-trimethylbenzoyl)benzoic acid (3·1 g.), m. p. 209—211°. Recrystallisation from benzene–light petroleum raised the m. p. to 212°.

(b) *Equimolecular quantities in the presence of* m-*xylene.* Silver perchlorate (0·025 mole) in *m*-xylene (60 c.c.) was added in 15 min. at 5° to a mixture of phthaloyl chloride (0·025 mole) and *m*-xylene (25 c.c.). After 0·5 hr. the reaction was stopped and worked up as above, to give *o*-(2 : 4-dimethylbenzoyl)benzoic acid (1·4 g.), m. p. 141°.

(c) *With two equivalents of silver perchlorate in the presence of* m-*xylene.* Phthaloyl chloride (0·025 mole) in nitromethane (25 c.c.) was added in 10 min. at 5° to silver perchlorate (0·05 mole) in nitromethane (60 c.c.) and *m*-xylene (15 c.c.). After 1 hr. the reaction was stopped. From the part (3·4 g.) of the product soluble in sodium hydrogen carbonate solution, *o*-(2 : 4-dimethylbenzoyl)benzoic acid (0·46 g.), m. p. 141°, was obtained as before.

(d) *In the presence of anisole.* Silver perchlorate (0·05 mole) in anisole (45 c.c.) was added in 3 min. at 0—5° to phthaloyl chloride (0·05 mole) and anisole (15 c.c.). After 0·5 hr. the silver chloride was filtered off and the filtrate washed with 2N-sodium hydroxide solution. The neutral portion (12·3 g.) of the product crystallised after the removal of the solvents, to give di-*O*-methylphenolphthalein (5·1 g.), m. p. and mixed m. p. 98—99°.

(e) *In nitromethane alone.* Silver perchlorate (0·5 mole) in nitromethane (75 c.c.) was added in 3 min. at −15° to a mixture of phthaloyl chloride (0·05 mole) and nitromethane (25 c.c.). Silver chloride was precipitated, the supernatant liquor became green and small amounts of chlorine dioxide were evolved. Strong cooling was necessary during the addition of anisole (0·10 mole) during 4 min. After another 5 min. the silver chloride was filtered off and the mixture worked up as before. Phthalic anhydride (5·4 g.) and phthalic acid (1·2 g.) were recovered.

Reaction of Silver Perchlorate with Terephthaloyl Chloride.—Silver perchlorate (0·05 mole) in nitromethane (75 c.c.) was added, in 10 min., at 20° to terephthaloyl chloride (0·05 mole) and nitromethane (50 c.c.), and the resultant mixture kept for 10 min. before addition of anisole (0·15 mole). After a further 15 min. the silver chloride was filtered off, the filtrate falling on crushed ice. 1 : 4-*Di*-p-*methoxybenzoylbenzene* (6·8 g.), m. p. 236—238°, separated and was collected; more of this (0·7 g.) was obtained by crystallisation of the product from pyridine, after terephthalic acid had been removed from it with sodium hydrogen carbonate solution. Recrystallisation of the diketone from acetic acid and then pyridine (twice) gave fine needles, m. p. 238° (Found: C, 76·1; H, 5·4. $C_{22}H_{18}O_4$ requires C, 76·3; H, 5·2%).

Reaction of Silver Perchlorate with Succinyl Chloride.—(i) *In the presence of anisole.* Silver perchlorate (0·05 mole) in nitromethane (80 c.c.) was added in 10 min. to a mixture of succinyl chloride (0·05 mole), anisole (15 c.c.), and nitromethane (20 c.c.). After 1 hr. the silver chloride was filtered off from the intensely mauve solution, the filtrate being allowed to fall on crushed ice. The product obtained in the usual way, a viscous mass (11·8 g.), gave on distillation a clear yellow-orange oil, b. p. 210—280°/1 mm. (9·8 g.), which did not crystallise.

(ii) *With two equivalents of silver perchlorate in the presence of* m-*xylene.* Succinyl chloride (0·025 mole) in nitromethane (25 c.c.) was added in 5 min. at 0° to silver perchlorate (0·05 mole) dissolved in *m*-xylene (15 c.c.) and nitromethane (70 c.c.), and the mixture allowed to warm to room temperature during 1 hr. The silver chloride was then filtered off and the product worked up in the usual way. The acidic portion crystallised, to yield β-2 : 4-dimethylbenzoylpropionic acid (0·39 g.), m. p. 109°, mixed m. p. 112° with sample of m. p. 114°. The neutral portion (2·6 g.) crystallised to yield crude succinic anhydride (1·1 g.).

(iii) *With equimolecular quantities in the presence of* m-*xylene.* Silver perchlorate (0·05 mole) in nitromethane (70 c.c.) was added during 5 min. at 20° to a mixture of succinyl chloride (0·05 mole), *m*-xylene (15 c.c.), and nitromethane (15 c.c.). The silver chloride was filtered off from the green solution after a further hr. The product crystallised from ether, to give β-2 : 4-dimethylbenzoylpropionic acid (4·7 g.), m. p. 110—112°.

Formation of Anthraquinone.—*o*-Benzoylbenzoic acid (0·025 mole) in acetic acid (20 c.c.) was treated with anhydrous perchloric acid (0·05 mole) in acetic acid and heated under reflux for 6 hr. Removal of acidic products then left anthraquinone (0·22 g.), m. p. and mixed m. p. 285—286°.

Reaction of o-*Benzoylbenzoyl Chloride with Silver Perchlorate in the Presence of Anisole.*—*o*-Benzoylbenzoyl chloride (0·025 mole) in nitromethane (25 c.c.) was added in 3 min. to a cold (−10°) solution of silver perchlorate (0·025 mole) in nitromethane (40 c.c.) and anisole (10 c.c.).

After 30 min. the reaction was stopped and the product, a clear pale yellow oil (8·0 g.), obtained in the usual way, crystallised on being seeded with 3-*p*-methoxyphenyl-3-phenylphthalide. Recrystallisation from toluene gave the pure phthalide (6·7 g.), m. p. 86°; a further 1·1 g. were obtained from the mother-liquor.

Reactions of Succinic Anhydride with Anisole in the Presence of Perchloric Acid.—(i) *In the cold, with anhydrous perchloric acid.* Succinic anhydride (8 g.) in nitromethane (50 c.c.) and anisole (10 c.c.) was treated with 72% perchloric acid (2·1 c.c.) at 24°. The solution slowly warmed to 35°, became mauve, and deposited succinic acid. After 4 days at room temperature the mixture was poured into water and ether and washed with sodium hydrogen carbonate solution. The neutral part of the product, a thick brown oil (2 g.), was extracted with light petroleum (3 × 100 c.c.) to give a pasty mass (0·5 g.), which on crystallisation from ethanol yielded light yellow needles of *γγ-di*-p-*methoxyphenyl-γ-butyrolactone* (0·3 g.), m. p. 105°; subsequent recrystallisations raised the m. p. to 106° (Found: C, 72·1; H, 5·8%; *M*, 238. $C_{18}H_{18}O_4$ requires C, 72·4; H, 6·0%; *M*, 298).

(ii) *In refluxing nitromethane, with anhydrous perchloric acid.* The above experiment was repeated but the mixture was heated under reflux for 1 hr. The neutral part (7·3 g.) of the product, a thick dark brown oil, was extracted with light petroleum as before but no crystalline product was obtained.

(iii) *In refluxing nitromethane, with anhydrous perchloric acid in acetic acid.* Succinic anhydride (0·05 mole), in nitromethane (15 c.c.) and anisole (15 c.c.), was treated with anhydrous perchloric acid (0·05 mole) in acetic acid, and the solution heated under reflux for 5 hr. Succinic acid (1·5 g.), m. p. and mixed m. p. 179—180°, crystallised overnight.

We thank Imperial Chemical Industries Limited for a grant.

QUEEN ELIZABETH COLLEGE (UNIVERSITY OF LONDON),
LONDON, W.8.

[*Received, November 1st,* 1956.]

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328. *Experiments in the* cyclo*Butane Series. Part II.*[1]

By F. B. KIPPING and J. J. WREN.

Perkin's bromination of *cis-cyclo*butane-1 : 2-dicarboxylic anhydride has been re-investigated, together with debromination of the products. Experiments directed to the synthesis of tetrahydroanemonin from *cyclo*butene-1 : 2-dicarboxylic acid are described.

IN Part I [1] preliminary experiments towards an unambiguous synthesis of anemonin were described. This paper deals with experiments directed to a synthesis of tetrahydroanemonin, which presumably has the same carbon skeleton as anemonin, but in which that skeleton is apparently more stable; for example, basic reagents cleave the *cyclo*butane ring of anemonin, but the tetrahydro-compound undergoes reversible basic hydrolysis.[2] Synthesis would confirm the structure of anemonin and show whether the spirolactone groupings are *cis*- or *trans*-related to one another. It has recently been realised that, whereas in the *cyclo*butyl anion [3] and radical [4] the ring is stable, in the *cyclo*butyl cation it is not [4,5] and consequently any reaction which involves generation of a *cyclo*butyl cation yields a mixture of products and is therefore unsuitable for an unambiguous synthesis. It seemed, therefore, that the crucial step in the synthesis of tetrahydroanemonin should be the stereospecific hydroxylation of an appropriate 1 : 2-disubstituted *cyclo*butene and that Perkin's *cyclo*butene-1 : 2-dicarboxylic acid [6] would be a suitable starting material.

[1] Alberman and Kipping, *J.*, 1951, 779.
[2] Asahina and Fujita, *Acta Phytochim.* (*Japan*), 1922, **1**, 1.
[3] Hamlin and Biermacher, *J. Amer. Chem. Soc.*, 1955, **77**, 6376.
[4] Roberts and Mazur, *ibid.*, 1951, **73**, 3542.
[5] Dewar, *Ann. Reports*, 1951, **47**, 120; Roberts and Mazur, *J., Amer. Chem. Soc.*, 1951, **73**, 2509; Roberts and Chambers, *ibid.*, p. 5034; Roberts and Simmons, *ibid.*, p. 5487; Applequist and Roberts, *ibid.*, 1956, **78**, 874.
[6] Perkin, *J.*, 1894, 950.

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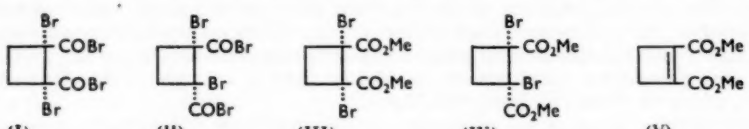
Bromination of *cis-cyclo*butane-1 : 2-dicarboxylic anhydride afforded a mixture of *cis-* (I) and *trans*-1 : 2-dibromo*cyclo*butane-1 : 2-dicarbonyl bromide (II). Solvolysis of this mixture, with silver acetate in 1 : 1 acetic acid–acetic anhydride, gave a complex mixture, from which neither the *cis-* nor the *trans*-tetra-acetoxy-derivative could be isolated; this confirmed the unsuitability of reactions involving *cyclo*butyl cations. Water converted the acid bromide mixture into a product from which *cis*-1 : 2-dibromo*cyclo*butane-1 : 2-dicarboxylic anhydride was obtained by distillation, and from it the corresponding acid as described by Perkin; the *trans*-acid sublimed from the residue after



distillation. Treatment of the acid bromide mixture with methanol and subsequent crystallisation afforded Perkin's crystalline dimethyl 1 : 2-dibromo*cyclo*butane-1 : 2-dicarboxylate, which has now been shown to be the *trans*-isomeride (IV). Perkin therefore isolated the *cis*-acid but the *trans*-ester. The *cis*-ester (III) was obtained from the mother-liquor, for the first time in crystalline form. A number of attempts to hydrolyse the esters to the respective acids, and also to prepare them from the acids gave inhomogeneous products, presumably owing to solvolysis of their labile tertiary bromine atoms.

Boiling ethanolic potassium iodide smoothly debrominated the *trans*-dibromide (IV), giving dimethyl *cyclo*butene-1 : 2-dicarboxylate (V), but it had no action on the *cis*-dibromide (III) which liberated no iodine from potassium iodide even in boiling butan-1-ol, and although some reaction occurred in boiling diethylene glycol or in methanol at 225° the products were mixtures. Preferred *trans*-elimination of bromine from vicinal dibromides in the presence of iodide ion is well known,[7] and therefore provides strong evidence for the configurations here assigned to the isomeric dibromides. In passing, it is interesting that Ellingboe and Fuson [8] apparently assigned the wrong configurations to the isomeric 1 : 2-dibenzoyl-1 : 2-dibromo*cyclo*butanes; the higher-melting isomeride (m. p. 155—156°) was called the *trans*, yet it was debrominated in the presence of iodide ion much less readily than the other (m. p. 111—112°). Both eventually yielded 1 : 2-dibenzoyl*cyclo*butene which gave, as would be expected, *cis*-1 : 2-dibenzoyl*cyclo*butane when it was catalytically hydrogenated, but when brominated (which should give *trans*-addition) gave the lower-melting dibromide. Modern knowledge of these reactions thus shows that the lower-melting dibromide must be the *trans*-isomeride.

Although remarkably inactive towards iodide ions the *cis*-dibromide (III) was debrominated with zinc, but this change was accompanied by varying amounts of reduction, depending on the solvent employed, and in anhydrous methanol, for example, only the reduction product, dimethyl *trans-cyclo*butane-1 : 2-dicarboxylate, was formed. Kon and Nandi [9] treated a mixture of the diethyl esters corresponding with (III) and (IV) with zinc dust in boiling ethanol, which indeed appears to be the best solvent for debromination of the *cis*-isomeride (III), but they were apparently unaware that reduction occurs simultaneously with debromination and that the *trans*-isomeride in their mixture was probably unaffected; in our hands the *trans*-isomeride (IV) failed to react with zinc dust in boiling ethanol. Kon and Nandi mention that the same method was used on the dimethyl esters, but not whether dimethyl *cyclo*butene-1 : 2-dicarboxylate (V) was obtained crystalline; in fact it would appear that their liquid products were impure.

[7] Winstein, Pressman, and Young, *J. Amer. Chem. Soc.*, 1939, **61**, 1645; Alexander, "Ionic Organic Reactions," John Wiley and Sons, Inc., New York, 1950, p. 118; Cornubert and Rio, *Compt. rend.*, 1954, **238**, 867; Goering and Espy, *J. Amer. Chem. Soc.*, 1955, **77**, 5023; Barton, *Quart. Rev.*, 1956, **10**, 50.
[8] Ellingboe and Fuson, *J. Amer. Chem. Soc.*, 1934, **56**, 1774.
[9] Kon and Nandi, *J.*, 1933, 1628.

Conversion of the *cyclo*butene ester (V) into the *trans*-dibromo-compound (IV) provides comfirmatory evidence of the configurations assigned above, and the structure of *cyclo*butene-1 : 2-dicarboxylic acid, obtained by hydrolysis of the ester, was confirmed by catalytic hydrogenation to *cis-cyclo*butane-1 : 2-dicarboxylic acid. The *cyclo*butene acid was also reconverted into its dimethyl ester *via* the dicarbonyl chloride.

It has not been possible to prepare an anhydride of *cyclo*butene-1 : 2-dicarboxylic acid.[6,10] When it was covered with acetyl chloride, the finely powdered acid did not dissolve until it was warmed and was then converted into the dicarbonyl chloride. Ethereal thionyl chloride and pyridine at 0° [11] also failed to convert it into the anhydride. When it was kept at 65° for nine days in pure acetic anhydride containing a trace of pyridine, or for shorter periods in boiling acetic anhydride or in a vacuum-sublimation apparatus at 200°, it was converted into rather involatile oils. These observations may be explained by assuming that too much ring strain would be present in the anhydride and also by Vogel's recent observation [12] that the ester (V) undergoes thermal cleavage to give dimethyl fulgenate (VI; R = Me): he converted the ester (V) into the Diels–Alder adduct of dimethyl fulgenate with maleic anhydride. It was at first considered surprising that the literature apparently contains no reference to fulgenic acid (VI; R = H), its anhydride or its esters, but presumably these compounds would polymerise very readily, being both dienes and dienophils (a similar explanation has been advanced for the absence of derivatives of buta-1 : 3-diene-2-carboxylic acid from the literature [13]). Perkin obtained " a new acid " by the action of water on the oily product of heating the *cyclo*butene acid, and this was probably a polymeride of fulgenic acid.

trans-Hydroxylation of the *cyclo*butene acid was attempted in the hope of preparing the dihydroxy-dicarboxylic acid which might, with suitable protection of the hydroxyl groups, be twice bishomologated by the Arndt–Eistert procedure to give an acid which would lactonise to tetrahydroanemonin or its geometrical isomeride. Organic peroxides, the conventional reagents for *trans*-hydroxylation of olefinic double bonds, are unsuitable for αβ-unsaturated acids,[14] but maleic acid has been successfully *trans*-hydroxylated by using aqueous hydrogen peroxide in the presence of pertungstic acid.[15] This method was therefore applied to the *cyclo*butene acid, but only succinic acid was formed. A similar cleavage of the *cyclo*butane ring was observed by Wille,[16] who converted the ester (V) into dimethyl 1 : 4-dioxoadipate with hydrogen peroxide and osmium tetroxide.

Application of the Arndt–Eistert synthesis to the *cyclo*butene acid was next investigated. Although carboxylic acids containing isolated double bonds can be successfully homologated [17,18] considerable difficulties arise with αβ-unsaturated acids. For example, even at −78° crotonyl chloride with diazomethane gives a pyrazoline diazoketone, which decomposes very readily with evolution of nitrogen.[18] However, a good yield of the diazoketone can be obtained from α-methylcinnamoyl chloride, although some of the pyrazoline diazoketone (VII; R = Me) is also formed; the diazoketone was converted by the Wolff rearrangement into the methyl ester of the homologous acid.[19] Cinnamoyl chloride yields corresponding products,[18-20] but a polymeride resulted from attempted Wolff rearrangement of the diazoketone. In the case of *cyclo*butene-1 : 2-dicarbonyl chloride the only isolable product was the pyrazoline diazoketone (VIII), the

[10] Wren, *J.*, 1956, 2208.
[11] Gerrard and Thrush, *J.*, 1952, 741.
[12] Vogel, *Angew. Chem.*, 1956, **68**, 189.
[13] Braude and Evans, *J.*, 1956, 3238.
[14] Boeseken, *Rec. Trav. chim.*, 1926, **45**, 838; English and Gregory, *J. Amer. Chem. Soc.*, 1947, **69**, 2120; Swern, *Chem. Rev.*, 1949, **45**, 50.
[15] Mugdan and Young, *J.*, 1949, 2988; Church and Blumberg, *Ind. Eng. Chem.*, 1951, **43**, 1780.
[16] Wille, *Annalen*, 1939, **538**, 237.
[17] Bachmann and Struve, " Organic Reactions," Vol. I (1942), p. 38.
[18] Wotiz and Buco, *J. Org. Chem.*, 1955, **20**, 210.
[19] Moore, *ibid.*, p. 1607.
[20] Cf. Bradley and Schwarzenbach, *J.*, 1928, 2904.

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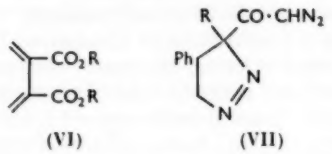
structure of which was proved by its infrared spectrum, and more particularly by its ultraviolet spectrum which is not that of an αβ-unsaturated diazoketone, as is shown in Table 1. Using varying dilutions of reactants, experiments were conducted at 0°, at



(VI) (VII) (VIII)

−80°, and at −105° : the mother-liquors after crystallisation of the pyrazolone diazoketone showed weak absorption maxima at 330—345 mμ, which suggested the presence of small amounts only of the desired 1 : 2-bisdiazoacetyl*cyclo*butene.

TABLE 1. *Ultraviolet spectra of diazoketones.*

Compound	$\lambda_{max.}$ (mμ)	ε	Solvent	Source
$(CH_2{\cdot}CH_2{\cdot}CO{\cdot}CHN_2)_2$	248·5	18,200	EtOH	Present work
	270·5	17,370		
(−)-$CH_3{\cdot}CH_2{\cdot}CHMe{\cdot}CO{\cdot}CHN_2$	250	8,800	EtOH?	Ref. 21
	267 *	7,600		
(+)-$Ph{\cdot}CH_2{\cdot}CHMe{\cdot}CO{\cdot}CHN_2$	250	9,500	,,	,,
	270 *	7,700		
Long-chain aliphatic diazoketones ...	247	10,500	PrⁱOH	Ref. 22
$Ph{\cdot}CH{:}CMe{\cdot}CO{\cdot}CHN_2$	276 *	16,000	EtOH	Ref. 19
	304	18,500		
(VII; R = H)	255 *	9,000	,,	,,
	276	10,400		
(VII; R = Me)	273	10,500	,,	,,
*cyclo*Butane derivative (VIII)	257 *	14,050	,,	Present work
	281	19,630		

* Inflection.

If the double bond of the *cyclo*butene acid could be protected by the formation of a Diels–Alder adduct with anthracene the carboxyl function could then be twice bishomologated to give the adduct of anthracene with *cyclo*butene-1 : 2-dipropionic acid, which might then be dissociated [23] to give the dipropionic acid. The *cyclo*butene ester (V) was found to be rather unreactive as a dienophil. No adduct was formed when solutions in benzene, toluene, xylene, or dioxan were refluxed with anthracene during several days. Crystalline ester could be recovered from the benzene solution, but not from the others (nor could crystalline acid be obtained after hydrolysis), and this is attributed to the thermal cleavage mentioned above. The ester also failed to react with 2 : 3-dimethylbutadiene at room temperature. The activity of maleic anhydride as a dienophil has been correlated with enhanced ultraviolet absorption which it shows when it is dissolved in benzene.[24] The *cyclo*butene ester showed no enhanced absorption in benzene solution above 273 mμ, and addition of 0·1% of benzene to its methanolic solution caused no spectral change, thus apparently confirming its weakness as a dienophil.

Diene synthesis was therefore attempted by using the more reactive pentacene instead of anthracene. The desired adduct has been obtained, but so far only in small yield based on the ester used. An isomeric adduct was also obtained when the ester was added

[21] Wiberg and Hutton, *J. Amer. Chem. Soc.*, 1956, **78**, 1640.
[22] Vandenheuvel and Yates, *Canad. J. Res.*, 1950, **25**, *B*, 556.
[23] Diels and Friedrichsen, *Annalen*, 1934, **513**, 145; Diels and Thiele, *Ber.*, 1938, **71**, 1173; Bartlett and Tate, *J. Amer. Chem. Soc.*, 1953, **75**, 91; Baumgartner and Hugel, *Bull. Soc. chim. France*, 1954, 1005; Applequist and Roberts, Abs. 128th Meeting, Amer. Chem. Soc., 1955, 62-O; *J. Amer. Chem. Soc.*, 1956, **78**, 4012.
[24] Barb, *Trans. Faraday Soc.*, 1953, **49**, 143; Andrews and Keefer, *J. Amer. Chem. Soc.*, 1953, **75**, 3776.

to a solution of pentacene in boiling nitrobenzene, and this appears to be derived from dimethyl fulgenate.

Experimental

M. p.s are corrected, b. p.s uncorrected. Infrared spectra were examined in Nujol mull, and ultraviolet spectra on Unicam S.P. 500 spectrophotometers.

Bromination of cis-cyclo*Butane*-1 : 2-*dicarboxylic Anhydride*.—Anhydride (40 g.) was converted into the mixture of dibromo-dicarbonyl bromides (I and II) (b. p. 104—117°/0·4 mm.).[6] The crude mixture was poured into anhydrous methanol (300 ml.) in a cooled 1-l. flask fitted with an efficient reflux condenser. Excess of methanol was evaporated, the residue shaken with water (2 l.) and ether, and the ethereal layer washed successively with aqueous sodium hydrogen sulphite, aqueous sodium carbonate, and water, dried ($CaCl_2$), and evaporated to give the crude mixture of dibromides (III and IV) (94·2 g., 90%), which partly solidified. Crystallisation from methanol (charcoal; 2 crops) yielded nearly colourless plates of the *trans*-dibromide (IV) (46 g., 44%); the pure material (40 g.), obtained after further crystallisation from methanol (charcoal) and light petroleum (b. p. 60—80°), had m. p. 87—87·5° (Perkin gave m. p. 88—89°) (Found: C, 29·1; H, 2·9. Calc. for $C_8H_{10}O_4Br_2$: C, 29·1; H, 3·1%). Its infrared spectrum showed bands at 1730 (s; C:O str.) and 924 cm.$^{-1}$ (m; *cyclo*butane? [25]).

The mother-liquor yielded no further crystals, and after evaporation was treated with ethanolic potassium iodide (see below); the product gave the cis-*dibromide* (III) (16·3 g., 15%) from ether at −40°; recrystallisation from ether afforded colourless rods, m. p. 41—42° (Found: C, 29·4; H, 3·1. $C_8H_{10}O_4Br_2$ requires C, 29·1; H, 3·1%). Its infrared spectrum showed bands at 1724 (s) and 918 cm.$^{-1}$ (m). Without the potassium iodide treatment, the *cis*-dibromide could be obtained from ether at −40°, but less pure.

The remaining mixture of *cyclo*butene ester (V) and *cis*-dibromide could not easily be separated by distillation, and was therefore treated with zinc dust in boiling ethanol (see below), and the product distilled. An almost colourless oil (b. p. 77—97°/1·0 mm.) was thus obtained, which solidified at −40° but melted again at room temperature; it consisted of dimethyl *cyclo*butene- and dimethyl *cyclo*butane-dicarboxylate, and its ultraviolet spectrum ($\lambda_{max.}$ 235 mμ, ε 6890, in MeOH) indicated that about 80% of the former was present. Hydrolysis (see below) yielded *cyclo*butene-1 : 2-dicarboxylic acid (4 g., 9%), and the mother-liquor from its crystallisation was shown by paper chromatography to contain *trans-cyclo*butane-1 : 2-dicarboxylic acid. It was calculated that the reaction had produced roughly 25% of *cis*- and 75% of *trans*-dibromide.

cis- *and* trans-1 : 2-*Dibromo*cyclo*butane*-1 : 2-*dicarboxylic Acid*.—A distilled mixture of the dibromo-dicarbonyl bromides was dissolved in warm aqueous acetone, and the solution evaporated. When the solid residue was heated at 170°/0·5 mm. *cis*-1 : 2-dibromo*cyclo*butane-1 : 2-dicarboxylic anhydride distilled. Crystallised from anhydrous benzene it formed colourless rods, m. p. 103—104° (Perkin gives m. p. 103—104°) (Found: C, 25·5; H, 1·25. Calc. for $C_6H_4O_3Br_2$: C, 25·4; H, 1·42%). Its infrared spectrum showed a strong doublet, 1822 and 1805 cm.$^{-1}$, characteristic of the anhydride grouping. It dissolved in boiling water and, on cooling, colourless hexagons of the pure *cis*-acid were deposited; they had m. p. 204—205° (sintered above 190°) [Perkin gives m. p. 202—205° (decomp.)] (Found: C, 24·0; H, 2·1. Calc. for $C_6H_6O_4Br_2$: C, 23·9; H, 2·0%). Its infrared spectrum showed strong bands at 2640, 2520, 1735, 1707, 1690, and 1672 cm.$^{-1}$. After the *cis*-anhydride has ceased to distil the temperature of the residue was raised to 210° and trans-1 : 2-*dibromo*cyclo*butane*-1 : 2-*dicarboxylic acid* sublimed from it. The acid formed colourless prisms, m. p. 247·5—248° (sintered above 190°) from xylene (Found: C, 24·1; H, 1·9. $C_6H_6O_4Br_2$ requires C, 23·9; H, 2·0%); its infrared spectrum showed strong bands at 2645, 2520, and 1705 cm.$^{-1}$.

Debromination of Dimethyl trans-1 : 2-*Dibromo*cyclo*butane*-1 : 2-*dicarboxylate* (IV).—The pure dibromide in ethanol was treated with powdered potassium iodide according to Perkin's directions; the colourless prisms of dimethyl *cyclo*butene-1 : 2-dicarboxylate (V), crystallised from light petroleum (b. p. 40—60°), had m. p. 45—46° (Perkin gives m. p. 44—46°), $\lambda_{max.}$ 232 mμ (ε 8700, in MeOH) (Found: C, 56·4; H, 5·9. Calc. for $C_8H_{10}O_4$: C, 56·5; H, 5·9%). Its infrared spectrum showed bands at 1735 (C:O str.) and 1635 cm.$^{-1}$ (C:C str.).

cyclo*Butene*-1 : 2-*dicarboxylic Acid*.—The pure ester (V) was digested for 20 min. with

[25] Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1954, pp. 28—29.

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excess of alcoholic potassium hydroxide. After evaporation the residue was shaken with water and ether, and the aqueous layer acidified with hydrochloric acid and continuously extracted overnight. Evaporation of the ethereal extract left colourless crystals, m. p. 174·5—177·5° after crystallisation from water (yield 75%). Further crystallisation from water or dioxan gave plates of the pure acid, m. p. 178—178·5° (decomp.) [Perkin gives m. p. 178° decomp.)] (Found : C, 51·0; H, 4·3. Calc. for $C_6H_6O_4$: C, 50·7; H, 4·3%). Its infrared spectrum showed bands at 2600(m), 2470(m), 1695(s), 1650(mw), and 1590 $cm.^{-1}$ (s). Its ultraviolet spectrum ($\lambda_{max.}$ 235 mμ, ε 10,600, in H_2O) shows an auxochromic effect due to the *cyclo*butene ring.[10] Dehydronorcaryophyllenic acid (3 : 3-dimethyl*cyclo*butene-1 : 2-dicarboxylic acid) has $\lambda_{max.}$ 238·5 mμ (ε 11,300, in H_2O), and so shows a similar auxochromic effect, enhanced by a second-order contribution of the *gem*-dimethyl groups. We are grateful to Professor H. N. Rydon for supplying a specimen of this acid (m. p. 194—195° after sintering).

Debromination of Dimethyl cis-1 : 2-*Dibromo*cyclo*butane*-1 : 2-*dicarboxylate* (III) *by Zinc Dust in Boiling Solvents.*—In none of the solvents used did a spontaneous reaction occur at room temperature (contrast Berson and Swidler,[26] etc.). No debromination occurred in anhydrous benzene or xylene (2 hr.), but it was effected, together with extensive reduction, in glacial acetic acid and in propan-1-ol. Less reduction occurred in commercial methanol (impure *cyclo*butene ester could be crystallised at −40°), but in anhydrous methanol reduction was exclusive : paper chromatography of the product after hydrolysis revealed none of the *cyclo*butene ester, but only *trans-cyclo*butane-1 : 2-dicarboxylic acid. The latter was isolated from the product of the acetic acid experiment in the following way : the product (3·0 g.) was heated at 210° for 7 hr. in a sealed tube with concentrated hydrochloric acid (10 ml.); the resulting brownish solution was boiled with charcoal, filtered, and evaporated, and the residue crystallised from benzene–dioxan (twice) and benzene (twice), giving colourless *trans*-acid (0·5 g., 25%), m. p. (and mixed m. p.) 130—131°.

Ethanol proved to be the most satisfactory solvent, as the following experiment (after Kon and Nandi) shows : Zinc dust (0·4 g.) was added in five roughly equal portions during 1 hr. to a stirred and refluxing solution of the *cis*-dibromide (1·0 g.) in ethanol (8 ml.). After a further hour the mixture was cooled, filtered, and evaporated. Addition of water then gave a little precipitate which was dissolved on the addition of a few drops of acetic acid. After two extractions of the product with ether the extracts were combined, dried ($CaCl_2$), and evaporated, yielding a colourless oil which gave crystals of the *cyclo*butene ester (V), m. p. *ca.* 30°, from ether–light petroleum (b. p. 60—80°) at −40°. Distillation of the oil failed to separate its components; hydrolysis afforded crystalline *cyclo*butene acid and some *trans-cyclo*butane-1 : 2-dicarboxylic acid (paper chromatogram).

Application of this method of debromination to the *trans*-dibromide (IV) gave interesting results : when acetic acid or anhydrous methanol was used the products were the same as from the *cis*-dibromide, but with ethanol the starting material was recovered unchanged.

Paper Chromatography of Hydrolysates containing cyclo*Butene*-1 : 2-*dicarboxylic Acid.*—Whatman No. 54 paper was used, with cineole (25 ml.), *tert.*-butyl alcohol (25 ml.), formic acid (*d* 1·2; 5 ml.), and water (5 ml.) as the mobile phase. After development (ascending; 2 days) the paper was dried at 100° for 1 day and examined under ultraviolet light : the *cyclo*butene acid then showed as a dark spot. Bromocresol-green spray was then used to reveal all acid spots. In model experiments on the pure acids the following R_F values were found : *cyclo*butene acid, 0·67—0·72; *cis-cyclo*butane-1 : 2-dicarboxylic acid, 0·73—0·79; *trans-cyclo*butane-1 : 2-dicarboxylic acid, 0·81—0·86. All hydrolysates from reactions of the *cis*-dibromide (III) with zinc contained the *trans*-acid, but in none was the *cis*-acid detected with certainty.

Addition of Bromine to Dimethyl cyclo*Butene*-1 : 2-*dicarboxylate.*—Excess of the ester was dissolved in an anhydrous solution of bromine in carbon tetrachloride (Perkin used bromine vapour). The colour of the bromine had not disappeared overnight, but was slowly discharged when the solution was boiled; more bromine was added until the reaction was complete. The product after evaporation was crystallised from methanol; it had m. p. and mixed m. p. with *trans*-dibromide (IV), 86—87°.

Catalytic Hydrogenation of cyclo*Butene*-1 : 2-*dicarboxylic Acid.*—The acid (0·2 g.) in " AnalaR " acetic acid (7 ml.) was shaken for 10 hr. with a little platinic oxide in hydrogen at atmospheric pressure and temperature. The product was filtered and evaporated, and the

[26] Berson and Swidler, *J. Amer. Chem. Soc.*, 1954, **76**, 4057.

residue crystallised from ether–benzene, giving *cis-cyclo*butane-1 : 2-dicarboxylic acid, m. p. and mixed m. p. 138—140°.

Attempted trans-*Hydroxylation of* cyclo*Butene*-1 : 2-*dicarboxylic Acid.*—A filtered solution of tungstic oxide (10 mg.) in aqueous sodium hydroxide was acidified with concentrated hydrochloric acid, and the precipitate separated and washed four times with water by centrifugation. It was then dissolved in 100-vol. hydrogen peroxide (1 ml.) and added to the *cyclo*butene acid (1·0 g.) in water (20 ml.) at 85—90°. Drops of the solution were tested periodically with potassium iodide, further portions of peroxide being added when necessary. After 5 hr. (total, 8 ml. of peroxide added) all the *cyclo*butene acid had reacted since the solution no longer showed any absorption maximum at 235 mμ. Excess of peroxide was then destroyed at 100° and the solution evaporated to small bulk; succinic acid (0·46 g.) crystallised (m. p. 188°). Its identity was confirmed by its infrared spectrum and by the diphenacyl ester, m. p. 151—151·5° (lit.,[27] 147·5°, uncorr.).

cyclo*Butene*-1 : 2-*dicarbonyl Chloride.*—Prepared from the acid by refluxing it for 3 hr. with thionyl chloride, the chloride had b. p. 65°/1·0 mm. (70% yield). Atmospheric moisture rapidly hydrolysed it to the acid; with methanol it yielded the ester (V), m. p. and mixed m. p. 43·5—45°.

Reaction of cyclo*Butene*-1 : 2-*dicarbonyl Chloride with Diazomethane.*—The chloride (467 mg.) in dry ether (20 ml.) was added rapidly to a vigorously stirred solution (100 ml.) of diazomethane (439 mg., 4 mol.) which had been distilled and dried over sodium.[28] Stored overnight at −40° the mixture deposited pale yellow crystals (201 mg.), which were separated and washed with ether by decantation. Crystallisation from ether gave pale yellow prisms of cis-3 : 4-*bisdiazoacetyl*-3 : 4-cyclo*butano*-Δ^1-*pyrazoline* (VIII), m. p. 137—138° (decomp.) (Found: C, 46·6; H, 3·3. $C_9H_8O_2N_6$ requires C, 46·5; H, 3·5%). Its infrared spectrum showed bands at 2116 (s; N_2 in diazoketone), 1623 (s; C:O str.), 1550 (m; N:N str.), and 920 cm.$^{-1}$ (w; *cyclo*butane?[25]); in related compounds[18,19,21,29] corresponding bands have been reported at 2270—2070 (N_2), 1645—1610 (C:O), and 1555—1550 cm.$^{-1}$ (N:N): see also 1 : 4-bisdiazoacetylbutane (below).

1 : 4-*Bisdiazoacetylbutane.*—Obtained[30] from pure benzene as slim pale yellow plates, m. p. 69—70°, this gave an infrared spectrum with characteristic bands at 2100 and 1622 cm.$^{-1}$.

Pentacene (cf. refs. 31—35).—4 : 6-Dibenzoyl-*m*-xylene, colourless prisms, m. p. 105·5—106° (lit.,[33] 104°), was prepared in 28% yield from *m*-xylene. Pyrolysis of this diketone induces an Elbs reaction followed by disproportionation, to give 6 : 13-(symmetrical)dihydropentacene and not pentacene itself. A number of experiments were made to discover the best pyrolysis temperature, the dihydropentacene from each being isolated by chromatography. A Pyrex boiling tube containing the diketone (5 g.) was immersed in a metal-bath at 450—460° during ¼ hr. After cooling, four such tubes were broken together and the hard black product extracted for 24 hr. with pure benzene (1·2 l.) in a universal extractor. The cooled extract was run on to an alumina column (750 g.; diam., 52 mm.) which was then developed with benzene. 6 : 13-Dihydropentacene formed a colourless zone (pale blue fluorescence in ultraviolet light) which was rapidly eluted, and obtained fairly pure from the pale yellow eluate (which fluoresced intensely pale blue). The yield was 7·9 g. (44%); once a yield of 62% was obtained. A specimen recrystallised twice from xylene and once from chloroform gave colourless jagged plates, m. p. 278—279° (lit.,[31] 273°), which fluoresced intensely pale blue in ultraviolet light (Found: C, 93·9; H, 5·7. Calc. for $C_{22}H_{16}$: C, 94·2; H, 5·8%). This fluorescence is rather surprising, being more characteristic of an anthracene than of a naphthalene structure. However, the ultraviolet spectrum is characteristic of a naphthalene structure, as Table 2 shows.

Dehydrogenation of 6 : 13-dihydropentacene, by phenanthrene-9 : 10-quinone in boiling nitrobenzene,[32] gave violet crystals of pentacene (25%) which were washed successively with nitrobenzene, ethyl acetate, and ether.

[27] Rather and Reid, *ibid.*, 1919, **41**, 75.
[28] *Org. Synth.*, Coll. Vol. II, p. 165.
[29] Bose and Yates, *J. Amer. Chem. Soc.*, 1952, **74**, 4703; ref. 25, p. 229.
[30] Walker, *J.*, 1940, 1304.
[31] Clar and John, *Ber.*, 1929, **62**, 3021.
[32] *Idem, ibid.*, 1930, **63**, 2967.
[33] *Idem, ibid.*, 1931, **64**, 981.
[34] Clar, John, and Hawran, *ibid.*, 1929, **62**, 940.
[35] Clar, *Chem. Ber.*, 1949, **82**, 495.

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Adduct of Pentacene with Dimethyl cyclo*Butane*-1 : 2-*dicarboxylate*.—A suspension of pentacene (0·22 g.) in pure benzene (20 ml.) containing the ester (2·0 g., 15 mol.) was heated in a sealed tube at 95° during 8 days. The product was filtered to remove traces of pentacene and brownish solid, and the filtrate evaporated, giving a viscous, orange-brown oil. None of the ester could be recovered from this oil by vacuum-sublimation. It slowly deposited rods (*ca.* 25 mg.) of the *adduct*, which was recrystallised from chloroform–light petroleum (b. p. 40—60°) and from methyl propionate, then having m. p. 278—278·5°; it showed a pale blue fluorescence in ultraviolet light, weaker than that of 6 : 13-dihydropentacene [Found : C, 80·2; H, 5·4%; *M* (Rast), 350. $C_{30}H_{24}O_4$ requires C, 80·3; H, 5·4%; *M*, 448]. Its ultraviolet spectrum (in $CHCl_3$) was similar to that of 6 : 13-dihydropentacene (see Table 2) : $\lambda_{max.}$ 272 (ε 17,750), 281·5 (ε 15,300), 309·5 (ε 1400), and 324·5 mμ (ε 1810); at 254 mμ, ε = 69,920. Its infrared spectrum showed one characteristic band at 1725 cm.$^{-1}$ (s; C:O str.). Both this and the adduct described below liberated pentacene when heated in capillary tubes with a naked flame.

Adduct of Pentacene with Dimethyl Fulgenate (*Buta*-1 : 3-*diene*-2 : 3-*dicarboxylate*).—Pentacene (440 mg.) was dissolved in boiling nitrobenzene (440 ml.), and the ester (total *ca.* 3 mol.) added

TABLE 2.

2 : 3-Dimethylnaphthalene (in 2-methylheptane) [36]		6 : 13-Dihydropentacene (in 2-methylheptane)		6 : 13-Dihydropentacene (in ethanol) [35]	
$\lambda_{max.}$ (mμ)	ε × 2	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε
—	—	214	50,600	—	—
226·5	287,800	235	186,000	234·5	144,500
—	—	261	10,400	261	11,500
268·5	9,820	270	12,200	271	12,900
278·5	10,440	279·5	12,000	281	11,800
288	7,020	290·5	7,640	292	7,240
302	790	—	—	—	—
306	930	305·5	1,760	305·5	1,580
315	556	315	786	315	794
320	706	320	1,690	319·5	1,450

portionwise until the colour of the solution changed from maroon to reddish-brown (20 min.). The solution was left to cool and then evaporated at 0·3 mm. on the water-bath, leaving a brown, partly solid residue which was dissolved in pure benzene (90 ml.); the filtered solution was run on to a column of neutral activated alumina (90 g., diam. 19 mm.). The column was developed with benzene and eluted in fractions. The first 525 ml. of eluate afforded minor quantities of oil; a colourless zone (3·5 cm.), which fluoresced intensely pale blue in ultraviolet light, then occupied the lower part of the column, and came off in the next 1300 ml. of eluate, evaporation of which left 360 mg. (53%) of the *adduct*. Recrystallised from methyl propionate it had m. p. 233·5—234·5° (decomp.), and fluoresced intensely pale blue in ultraviolet light [Found : C, 80·1; H, 5·3%; *M* (Rast), 343. $C_{30}H_{24}O_4$ requires C, 80·3; H, 5·4%; *M*, 448]. Its ultraviolet spectrum in $CHCl_3$ (cf. above and Table 2) had max. at 271·5 (ε 18,200), 280·5 (ε 15,600), 309 (ε 1500), 324 mμ (ε 1870); at 254 mμ, ε = 50,970. Its infrared spectrum showed bands at 1750 (s; C:O str. in ester), 1726 (s; C:O str. in αβ-unsaturated ester), and 1631 cm.$^{-1}$ (m.; C:C str., adjacent to carbonyl).

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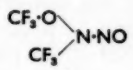
[36] A.P.I. Ultraviolet Spectrum, No. 222.

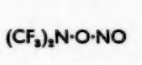
329. *Perfluoroalkyl Derivatives of Nitrogen. Part VI.* NN-Bistrifluoromethylhydroxylamine, the Structure of Trifluoronitrosomethane Dimer, and the Direction of Free-radical Addition to a Nitroso-group.†*

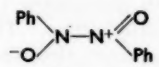
By R. N. Haszeldine and B. J. H. Mattinson.

Trifluoronitrosomethane dimer, produced photochemically from trifluoronitrosomethane, is shown by chemical and spectroscopic studies to be $(CF_3)_2N{\cdot}O{\cdot}NO$. Attack of a free CF_3 radical is thus on the nitrogen atom of the N:O group, and not on the oxygen as was tentatively concluded earlier. Reaction of *O*-nitrosobistrifluoromethylhydroxylamine (bistrifluoromethylhydroxylamine nitrite) with methanol or aqueous hydrogen chloride yields *NN*-bistrifluoromethylhydroxylamine. Phosphorus pentachloride converts the last compound into *N*-chlorobistrifluoromethylamine, which oxidises hydrogen chloride to chlorine and is itself reduced to bistrifluoromethylamine.

Trifluoronitrosomethane,[1] a deep-blue gas, yields an orange-red dimer [2] quantitatively when exposed to light. It was concluded [2] that the dimer was (I) or (II), and not a dimer analogous to that (III) of nitrosobenzene. Although initial infrared-spectroscopic studies [3] suggested that (I) was more probable than (II), further studies on the spectra


(I)


(II)


(III) (*cis or trans*)

of nitrosamines and nitrites,[4] and the synthesis of suitable reference compounds,[1] together with chemical evidence, now show that this was incorrect: *O*-nitrosobistrifluoromethylhydroxylamine (II) is the correct structure for the dimer of trifluoronitrosomethane.

Chemical Evidence.—Two procedures have proved successful for the conversion of the nitrite (II) into the parent hydroxylamine $(CF_3)_2N{\cdot}OH$. The strongly electronegative CF_3 groups make possible the equilibrium:

$$\underset{\text{B. p. } 10°}{(CF_3)_2N{\cdot}O{\cdot}NO} + CH_3{\cdot}OH \rightleftharpoons \underset{\text{B. p. } 35°\ \text{(predicted)}}{(CF_3)_2N{\cdot}OH} + \underset{\text{B. p. } -12°}{CH_3{\cdot}O{\cdot}NO}$$

and the volatility of methyl nitrite enables it to be removed by distillation as formed, so displacing the equilibrium; *NN*-bistrifluoromethylhydroxylamine was thus isolated (75% yield; b. p. 32·5°).

The reaction:

$$(CF_3)_2N{\cdot}O{\cdot}NO + HCl\ (aq.) \rightleftharpoons (CF_3)_2N{\cdot}OH + NOCl$$

is probably also an equilibrium, and removal of nitrosyl chloride by reaction with mercury enables *NN*-bistrifluoromethylhydroxylamine to be prepared more conveniently (72% yield) than by the first method.

The boiling point of bistrifluoromethylhydroxylamine (32·5°) suggests, by comparison with that of the amine $(CF_3)_2NH$ (−6·7°),[1] that hydrogen bonding is not very pronounced, despite the fact that the hydrogen will be more acidic than in, say, *NN*-dimethylhydroxylamine; the reduced basicity of the nitrogen and the oxygen is clearly more important,

* Part V, *J.*, 1957, 30.
† For a preliminary communication see *Chem. and Ind.*, 1956, 81.

[1] Barr and Haszeldine, *J.*, 1955, 1881, 2532, where earlier references are given.
[2] Haszeldine and Jander, *J.*, 1954, 696.
[3] *Idem*, *J.*, 1954, 691.
[4] Haszeldine and Mattinson, *J.*, 1955, 4172.

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and the situation resembles that in polyfluoro-alcohols.[5] The boiling point of *NN*-dimethylhydroxylamine [6] is 95°. *NN*-Bistrifluoromethylhydroxylamine is stable to an aqueous solution containing 5% (v/v) of concentrated hydrochloric acid, but is decomposed slowly by 2% aqueous sodium hydroxide to give fluoride and nitrite, possibly *via* initial elimination of fluoride : [1]

$$(CF_3)_2N{\cdot}OH \xrightarrow{NaOH} (CF_3)_2N{\cdot}O^-$$

$$CF_3{-}\overset{O^-}{\underset{\curvearrowright}{N^+}}{-}CF_2{-}F \longrightarrow CF_3{-}\overset{O^-}{N^+}{=}CF_2 \xrightarrow{OH^-} F^-, CO_3^{2-}, NO_2^-$$

The structure of *NN*-bistrifluoromethylhydroxylamine was proved by its reaction with phosphorus pentachloride to give the known [1] bistrifluoromethylamine in 80% yield. This eliminates the possibility that the compound of b. p. 32·5° was actually the compound $(CF_3)(CF_3{\cdot}O)NH$ arising by the reactions

$$(CF_3)(CF_3{\cdot}O)N{\cdot}NO + CH_3{\cdot}OH \rightleftharpoons (CF_3)(CF_3{\cdot}O)NH + CH_3{\cdot}O{\cdot}NO$$

$$(CF_3)(CF_3{\cdot}O)N{\cdot}NO + HCl \rightleftharpoons (CF_3)(CF_3{\cdot}O)NH + NOCl$$

since reaction with phosphorus pentachloride could clearly not convert this compound into bistrifluoromethylamine. The stability of the compound, b. p. 32·5°, to water and aqueous acid also proves that the compound $(CF_3)(CF_3{\cdot}O)NH$ is not present, since it is known [1] that compounds containing the $-CF_2{\cdot}NH-$ group are stable only in solvents of low dielectric constant and decompose in water by initial loss of hydrogen fluoride; by analogy with bistrifluoromethylamine, decomposition would occur as follows :

$$CF_3{\cdot}O{\cdot}NH{\cdot}CF_3 \xrightarrow{-HF} CF_3{\cdot}O{\cdot}N{:}CF_2 \xrightarrow{H_2O} CF_3{\cdot}O{\cdot}N{:}C{:}O$$

$$CF_3{\cdot}O{\cdot}N{:}C{:}O \xrightarrow{H_2O} CF_3{\cdot}O{\cdot}NH_2 \longrightarrow CF_3{\cdot}OH, NH_2{\cdot}OH, F^-, CO_3^{2-}$$

The formation of bistrifluoromethylamine by reaction of *NN*-bistrifluoromethylhydroxylamine with phosphorus pentachloride clearly involves the intermediate formation of *N*-chlorobistrifluoromethylamine; the two CF_3 groups make the chlorine atom in this compound extremely " positive," and the oxidation of hydrogen chloride explains the formation of free chlorine at 50° :

$$(CF_3)_2N{\cdot}OH + PCl_5 \longrightarrow (CF_3)_2NCl + POCl_3 + HCl$$

$$(CF_3)_2\overset{\delta-}{N}{-}\overset{\delta+}{Cl} + HCl \longrightarrow (CF_3)_2NH + Cl_2$$

Reaction of *NN*-bistrifluoromethylhydroxylamine with phosphorus pentachloride at room temperature liberates the theoretical amount of hydrogen chloride within a few minutes, and free chlorine begins to appear only after 1—2 hours or when the reactants are heated. The presence in the early stages of the room-temperature reaction of the reactive compound $(CF_3)_2NCl$ is apparent from qualitative tests and spectroscopic examination, but an attempt to separate it from the phosphorus oxychloride failed on the scale used, despite the predicted appreciable difference in boiling point. Reaction with mercury converts the *N*-chloro-compound into a compound of much higher molecular weight, doubtless tetrakistrifluoromethylhydrazine :

$$2(CF_3)_2NCl + Hg \longrightarrow (CF_3)_2N{\cdot}N(CF_3)_2 + HgCl_2$$

[5] Haszeldine, *J.*, 1953, 1757.
[6] Hepworth, *J.*, 1921, 251.

Bistrifluoromethylamine fails to react photochemically with chlorine, thus showing, not unexpectedly, that the equilibria :

$$(CF_3)_2NH \underset{HCl}{\overset{Cl\cdot}{\rightleftharpoons}} (CF_3)_2N\cdot \underset{h\nu}{\overset{Cl_2}{\rightleftharpoons}} (CF_3)_2NCl$$

lie to the left.

Spectroscopic Evidence.—Fluorine-free nitrosamines and nitrites can be distinguished by the marked shift to the blue which occurs for the nitrosamine spectrum as the solvent becomes more polar,[4] but clear-cut distinction cannot be made from vapour spectra alone. Fluorine in the β-position of a nitrosamine or nitrite causes a shift to the red of 6—10 mμ for the main ultraviolet maxima for the vapour,[4] but again distinction between the two cannot be made. However, the equilibrium :

$$R\cdot CH_2\cdot O\cdot NO + C_2H_5\cdot OH \rightleftharpoons R\cdot CH_2\cdot OH + C_2H_5O\cdot NO$$

lies well to the right when R = fluoroalkyl and the ultraviolet spectrum of a fluoroalkyl nitrite in ethanol is thus essentially that of ethanolic ethyl nitrite and quite different from the spectrum of the fluoroalkyl nitrite as a vapour or as a solution in light petroleum. By contrast, the ultraviolet spectrum of a fluoroalkylnitrosamine is scarcely altered by change from vapour to solution in ethanol and is quite distinct from that of ethyl nitrite.[4] Distinction between a nitrosamine and a nitrite each containing fluorine near to the N·NO or O·NO system can thus be made by observing if the spectrum remains virtually unchanged in ethanolic solution (fluoro-nitrosamine) or changes to that of ethyl nitrite (fluoro-nitrite).

The presence of the nitrite structure in trifluoronitrosomethane dimer is strongly suggested by the fact that the spectrum of its solution in light petroleum is essentially the same as that of the vapour (Table), whereas the spectrum of its ethanolic solution is identical with that of ethanolic ethyl nitrite [386 (infl.), 370, 357 (main peak), 345, 334, 324, and 314 mμ]. The shift to the red of the main nitrite peak observed for trifluoroethyl nitrite [4] is thus continued with *O*-nitrosobistrifluoromethylhydroxylamine : EtO·NO 355; $CF_3\cdot CH_2\cdot O\cdot NO$ 364; $(CF_3)_2N\cdot O\cdot NO$ 374 mμ.

Ultraviolet spectra (300—450 mμ).*

	$\lambda_{max.}$	ε	$\lambda_{min.}$	ε		$\lambda_{max.}$	$\lambda_{min.}$
$(CF_3)_2N\cdot O\cdot NO$	448	6·6	447	6·5	$CF_3\cdot CH_2\cdot O\cdot NO$	381	374
vapour	445	6·9	444	6·8	in light	364	358
	439	7·6	438	7·5	petroleum	351	344
	380	16·30	379	16·10		337	330
	374·5	16·70	374	16·60		325	320
	372	16·69	371	16·50		314 *	—
	368	16·60	367	16·40			
	366	16·60	322·5	8·6			
	317·5	9·64	316	9·3			

* See ref. 4 for vapour and solution spectra of $CF_3\cdot CH_2\cdot O\cdot NO$ and $(CF_3\cdot CH_2)_2N\cdot NO$.

Our further studies [4] on the infrared spectra of dialkylnitrosamines have shown that strong dipolar interaction occurs in the liquid or in solution with consequent marked shift of the N:O vibration [*e.g.*, $Me_2N\cdot NO$: vapour 6·72 μ (monomer); CCl_4 solution 6·88 μ (monomer), 7·63 μ (" dimer "); liquid 6·92 μ (monomer), 7·60 μ : (" dimer ")]. The original infrared spectroscopic evidence [3] for the structure of trifluoronitrosomethane dimer is thus invalidated, and it is now clear that the N:O vibration for (I) would lie between 5·9 and 6·4 μ [cf. $Me_2N\cdot NO$ 6·72 μ; $(CF_3\cdot CH_2)_2N\cdot NO$ 6·45 μ], where the trifluoronitrosomethane dimer actually shows only weak absorption. By contrast, extrapolation of the N:O vibration for EtO·NO (5·97 μ) and $CF_3\cdot CH_2\cdot O\cdot NO$ (5·76 μ) to $(CF_3)_2N\cdot O\cdot NO$ gives a predicted value for the N:O vibration of 5·4—5·7 μ, and the distinct doublet at

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5·47, 5·55 μ in the spectrum of trifluoronitrosomethane dimer is now to be assigned to the N:O vibration in *O*-nitrosobistrifluoromethylhydroxylamine.

Free-radical Addition to a Nitroso-group.—The elucidation of the structure of trifluoronitrosomethane dimer as *O*-nitrosobistrifluoromethylhydroxylamine establishes the direction of free-radical addition to a nitroso-group :

$$CF_3{\cdot}NO \xrightarrow{h\nu} CF_3{\cdot} + NO$$

$$CF_3{\cdot} + CF_3{\cdot}N{:}O \longrightarrow (CF_3)_2N{\cdot}O{\cdot}$$

$$(CF_3)_2N{\cdot}O{\cdot} + NO \longrightarrow (CF_3)_2N{\cdot}O{\cdot}NO$$

or

$$(CF_3)_2N{\cdot}O{\cdot} + CF_3{\cdot}NO \longrightarrow (CF_3)_2N{\cdot}O{\cdot}NO + CF_3{\cdot} \longrightarrow \text{etc.}$$

The CF_3 radical clearly attacks nitrogen in preference to oxygen. The nitroso-group in trifluoronitrosomethane, prevented from forming a dimer of the nitrosobenzene type (III), thus reacts in many ways like a C:C double bond, undergoing nucleophilic [1] or free-radical attack, and is capable o fgiving a $\cdots N{\cdot}O{\cdot}C{\cdot}C \cdots$ copolymer or an oxazetidine $-\overline{N-O-C-C}-$ with olefins.[1, 7]

Experimental

Preparation of O-Nitrosobistrifluoromethylhydroxylamine [NN-*Bistrifluoromethylhydroxylamine Nitrite*].—In a typical experiment, trifluoronitrosomethane (0·0566 mole) in a sealed 188-ml. silica tube was exposed to ultraviolet and visible radiation from a Hanovia arc for 40 hr. The lower 2″ of the tube were covered by black paper to shield liquid products from further irradiation. A small amount (*ca.* 0·0001 mole) of a non-condensable gas was discarded, and the reaction products were distilled *in vacuo*, to give unchanged trifluoronitrosomethane (0·0105 mole, 18%), carbon dioxide (0·0016 mole, 4%; separated from the trifluoronitrosomethane by treatment with aqueous sodium hydroxide), and O-*nitrosobistrifluoromethylhydroxylamine* (0·0221 mole, 96% based on $CF_3{\cdot}NO$ used) (Found : C, 12·0; N, 14·2%; *M*, 198. $C_2O_2N_2F_6$ requires C, 12·1; N, 14·1%; *M*, 198), b. p. 10°, as a red-brown liquid changing to a yellow solid when cooled. Over-irradiation caused some formation of dinitrogen tetroxide, but this may be removed by shaking the crude product with mercury before fractionation.

Bistrifluoromethylhydroxylamine.—Method A. Methanol (2·29 ml., 10% excess; dried by CaO under reflux, followed by Mg under reflux, then fractionated) was frozen in a 20-ml. flask fitted with a vertical condenser cooled over a 25 cm. length by ice–salt at −10°, leading to traps cooled by liquid oxygen. The apparatus was evacuated and *O*-nitrosobistrifluoromethylhydroxylamine (10·3 g., 0·0519 mole) was condensed into the flask; dry nitrogen was then admitted until the pressure reached atmospheric. The reactants were warmed to 0°, whereupon methyl nitrite (b. p. −12°) slowly began to condense in the traps. The reactants were gradually heated from 0° to 40° during 7 hr., and during the last hour unchanged *O*-nitrosobistrifluoromethylhydroxylamine was under reflux. The contents of the traps and the flask were fractionated separately, to give unchanged *O*-nitrosobistrifluoromethylhydroxylamine (0·0144 mole, 28%), methyl nitrite (0·0320 mole, 85%), *bistrifluoromethylhydroxylamine* (3·92 g., 62%), b. p. 32·5° (isoteniscope) (Found : C, 14·0; H, 0·7; N, 8·3%; *M*, 169. C_2HONF_6 requires C, 14·2; H, 0·6; N, 8·3%; *M*, 169), and a mixture of bistrifluoromethylhydroxylamine (0·005 mole) and methanol. The total yield of the bistrifluoromethylhydroxylamine based on the *O*-nitroso-compound used (72%) is thus 75%. It was not possible to separate methanol and bistrifluoromethylhydroxylamine by distillation on the scale used, and azeotrope formation is probable; final removal of methanol was effected by treatment thrice with an excess of " AnalaR " calcium chloride.

Method B. Mercury (1 ml.), aqueous hydrochloric acid (1·34 ml., containing 50% (v/v) of conc. acid 100% excess), and *O*-nitrosobistrifluoromethylhydroxylamine (0·774 g., 0·00391 mole) in a sealed Pyrex tube were allowed to warm from liquid-oxygen temperature to that of the room. Rapid reaction was apparent, the mercury was soon attacked, and the red-brown colour typical of the *O*-nitroso-compound faded to a pale yellow. The tube was then shaken

[7] Barr and Haszeldine, *Nature*, 1955, **175**, 991.

for 16 hr. without apparent change in colour. Fractionation gave bistrifluoromethylhydroxylamine (0·00280 mole, 72%) (Found: *M*, 169. Calc. for C_2HONF_6: *M*, 169), shown to be identical with the compound prepared by Method *A* by comparison of infrared spectra. A pale green liquid (0·0077 mole, equiv. to 20% of starting material) (Found: *M*, 202) and small amounts of hydrogen chloride, carbon dioxide, and nitric oxide were also isolated.

Reactions of Bistrifluoromethylhydroxylamine.—(a) *Stability to acid.* The hydroxylamine (0·406 g.) and aqueous hydrogen chloride (0·82 ml., concn. as above) formed two sharply defined layers when sealed *in vacuo* in a 5-ml. Pyrex tube. The tube was shaken vigorously (16 hr.) and the more volatile products were then fractionated *in vacuo*, to give unchanged bistrifluoromethylhydroxylamine (0·404 g., 99·5%) (Found: *M*, 169), whose identity was confirmed by infrared spectroscopy.

(b) *Stability to aqueous alkali.* Bistrifluoromethylhydroxylamine (0·345 g., 0·00204 mole) was shaken with 2% aqueous potassium hydroxide (8·4 ml.) in a sealed 25-ml. Pyrex tube for 20 hr. at 20°. The unchanged bistrifluoromethylhydroxylamine (39%) was removed by fractionation *in vacuo*, and the acidified (dilute sulphuric acid) aqueous solution gave positive tests for fluoride (cerous nitrate) and nitrite.

(c) *With phosphorus pentachloride.* Finely powdered phosphorus pentachloride (5·5 g., 350% excess) was placed in a 35-ml. Pyrex tube which was then pumped out (1 hr.) before bistrifluoromethylhydroxylamine (1·0 g., 0·00591 mole) was condensed in and the tube sealed. After 1·5 hr. at 20° only a faint yellow colour was apparent and after 3 hr. the tube was heated to 50° for 21 hr., then set aside at 20° for 20 hr. The intensity of the yellow colour had then increased appreciably. Fractionation in a vacuum-apparatus free from mercury showed chlorine to be a product. The residual chlorine was removed from the main volatile products by reaction with mercury, and refractionation gave bistrifluoromethylamine (0·00474 mole, 80%) (Found: N, 9·0%; *M*, 153. Calc. for C_2HNF_6: N, 9·2%; *M*, 153) spectroscopically identical with a known sample,[3] hydrogen chloride (Found: *M*, 38·5. Calc. for HCl: *M*, 36·5), and phosphorus oxychloride (0·81 g., 89%), identified by means of its infrared spectrum.

In a second experiment bistrifluoromethylhydroxylamine (0·82 g., 0·0049 mole), shaken with phosphorus pentachloride (5·5 g.) at 20° for 40 min., gave hydrogen chloride (99·5%) (Found: *M*, 37·0), phosphorus oxychloride, and a compound which is probably *N*-chlorobistrifluoromethylamine, but no chlorine. *N*-Chlorobistrifluoromethylamine is difficult to separate from phosphorus oxychloride on the scale used; it reacts rapidly with mercury to give mercuric chloride and a liquid of vapour pressure approx. 95 mm. at 20° and molecular weight *ca.* 300 believed to be tetrakistrifluoromethylhydrazine (*M*, 304).

Reaction of Bistrifluoromethylamine with Chlorine.—The amine (2·08 g., 0·0136 mole; prepared as described earlier) and chlorine (0·704 g., 0·0099 mole) were exposed to ultraviolet light in a 190-ml. silica tube for 71 hr. Removal of the chlorine by reaction with mercury and fractionation *in vacuo* gave only unchanged bistrifluoromethylamine (99%) (Found: *M*, 154. Calc. for C_2HNF_6: *M*, 153), and in particular there was no indication of the formation of tetrakistrifluoromethylhydrazine.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, July 18th*, 1956.]

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330. *The Infrared Spectra of Some Monocarboxylic Acids.*

By P. J. Corish and D. Chapman.

Infrared spectra in the region 3500—670 cm.$^{-1}$ have been obtained for the simple normal monocarboxylic acids including dodecanoic acid and acids of shorter chain length in the liquid and the crystalline state. Characterisation of these acids by means of their crystalline spectra has been made possible, and information on the dimeric form and also on the shape of the $[CH_2]_n$ chain has been deduced.

The infrared spectra of the crystalline forms of the longer-chain monocarboxylic acids (C_{14}—C_{21}) have been discussed by Sinclair *et al.*[1] and Jones *et al.*,[2] who pointed out the existence of characteristic groups of bands in the 1180—1350 cm.$^{-1}$ region which could be used as a means of identifying individual acids. In the present paper the infrared spectra of the lower members of the monocarboxylic acid series in the liquid and the crystalline state are presented and discussed. Such characterisation in the region 1180—1350 cm.$^{-1}$ has been extended, and supplemented by the finding of series of bands in the 900—720 cm.$^{-1}$ region.

Experimental

The acids examined had either been prepared in the Unilever or the Dunlop Research laboratories, *e.g.*, dodecanoic (m. p. 43·95°), decanoic (m. p. 30·6°), and octanoic (m. p. 16·4°), or were distilled fractions of good-quality commercial acids, *e.g.*, acetic (b. p. 118°), propionic (b. p. 141°), butyric (b. p. 163°), valeric (b. p. 186°), hexanoic (b. p. 202°), heptanoic (b. p. 211°), and nonanoic (b. p. 253°).

The spectra of acids crystalline at room temperature were obtained in the normal manner between rock-salt plates. The spectra of such acids in the liquid state were obtained by means of a heated cell.

For crystalline-state spectra the acids normally liquid at room temperature were obtained as capillaries by using a transmission-type low-temperature cell with solid carbon dioxide–alcohol and liquid nitrogen as refrigerants. The spectrometer was a Grubb-Parsons S.3. double-beam instrument.

The spectra are shown in Figs. 1 and 2.

Discussion

Spectral changes occurring on transition from the liquid to the crystalline state may be due to the effect of the imposed symmetry of the unit cell, to rotational isomerism, or to changes in hydrogen bonding. With respect to changes due to the symmetry of the unit cell, it is important to take polymorphism into account.

Even-membered fatty acids occur in three modifications, A, B, and C, giving different long spacings decreasing in that order. The fused even-membered acids, *e.g.*, dodecanoic, always crystallise in the C form.[3] This form has been shown to be of monoclinic symmetry with orthorhombic packing of the hydrocarbon chains. In dodecanoic acid the chains are considered to be bent and not strictly in the orthorhombic sub-cell.

The polymorphism of the odd-membered acids is more complex,[3] but the C′ form is always the first to separate from the molten acid and changes some 10—20° below the solidifying point into one or both of the forms A′ and B′. The A′-form is triclinic with the hydrocarbon chains packed roughly in the triclinic manner.[4] The chains are thought to be probably helically twisted in *n*-pentadecanoic and lower acids, but less twisted for the

[1] Sinclair, McKay, and Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 2570.
[2] Jones, McKay, and Sinclair, *ibid.*, p. 2575.
[3] Malkin, "Progress in the Chemistry of Fats and Other Lipids," Pergamon Press, London, 1952, Vol I, p. 10.
[4] von Sydow, *Acta Chem. Scand.*, 1955, **9**, 1119.

higher members. Form B′ has a symmetry similar to that of form A′, but the hydrocarbon chains are orthorhombically packed and deformed near the carboxyl groups;[4] there is unfortunately no information available for the lower members. It seems probable that the form from the melt for the odd-acids here examined will be the A′-form since this is the only form observed with tridecanoic acid.[4] Evidence about this for the lower members is not, however, available.

FIG. 1.

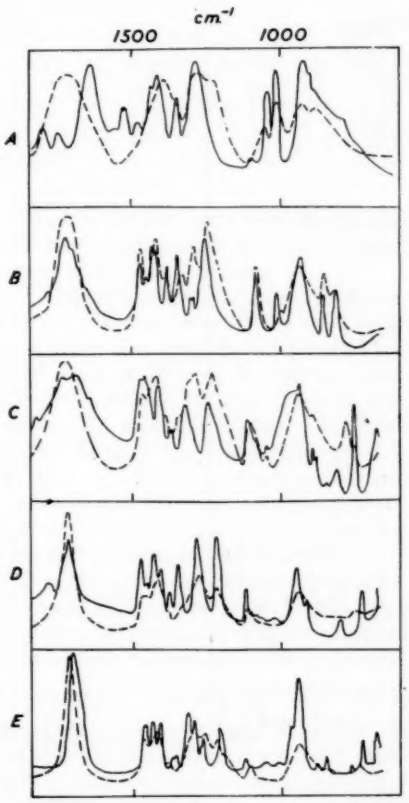
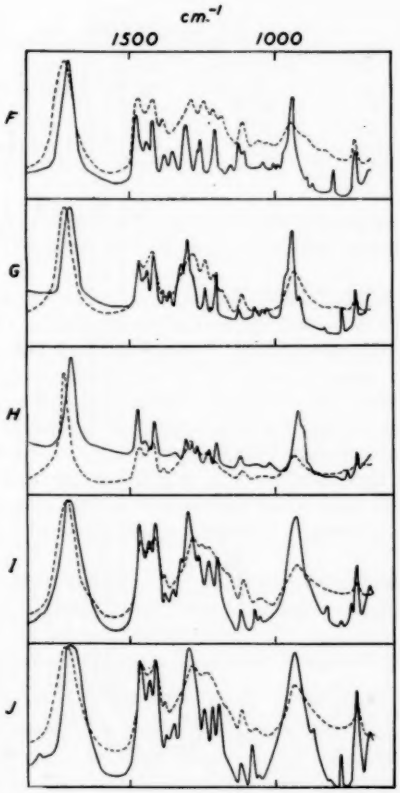


FIG. 2.



--- *Liquid.* —— *Solid.*

Acids: *A, acetic*; *B, propionic*; *C, butyric*; *D, valeric*; *E, hexanoic*; *F, heptanoic*; *G, octanoic*; *H, nonanoic*; *I, decanoic*; *J, dodecanoic.*

Therefore, when the spectra of the even and odd acids are compared, effects due to the different crystal structures may occur.

Figs. 1 and 2 show differences between the crystalline-state spectra of the even- and the odd-membered acids which may be due to this effect. Except acetic acid (which probably has a different crystalline form), all the even-membered acids show a band near 680 cm.$^{-1}$, and the odd-membered acids show an " analogous " band at a lower frequency. Further, the band near 1300 cm.$^{-1}$ (assigned to a dimeric carboxyl vibration) appears to alternate somewhat in frequency as we change from an odd- to an even-membered acid.

The type of effect imposed by the symmetry of the unit cell in the monocarboxylic

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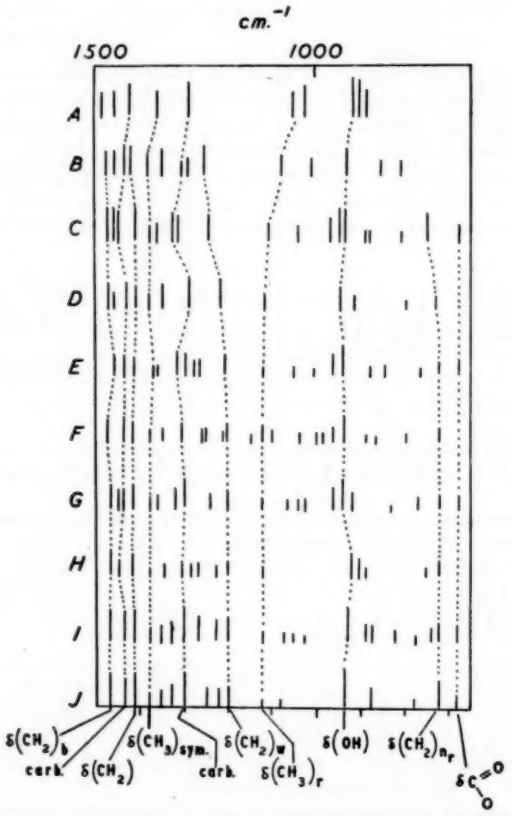
acids is perhaps illustrated by the spectrum of the B-form of stearic acid. It is of interest that, under certain conditions, decanoic acid also exhibits two C=O bands (see Appendix).

Comparison between spectra for the liquid and the crystalline state of the acids shows that the region between 700 and 1350 cm.$^{-1}$ becomes much less defined for the liquid state. (This is presumably due to an increase in the number of possible rotational isomers

FIG. 3.



Acids: A, acetic; B, propionic; C, butyric; D, valeric; E, hexanoic; F, heptanoic; G, octanoic; H, nonanoic; I, decanoic; J, dodecanoic.

in the liquid state, but it may also be that the thermal agitation in the liquid tends to make the twisting and the wagging modes of the additional CH_2 groups less well defined.)

It should be noted that *X*-ray investigation of these monocarboxylic acids in the liquid and the crystalline state [5] led to the conclusion that the molecules are not arranged in the same way in the two states.

In general, crystallisation results in only small shifts in the C=O frequencies, except with acetic acid (see Table 1). No odd–even alternation of the carbonyl frequency as reported by Sinclair *et al.*[1] was observed. Slight shifts and additional bands in the 2500—3000 cm.$^{-1}$ ν-OH region (OH stretching) also result from crystallisation. These shifts are

[5] Morrow, *Phys. Rev.*, 1928, **31**, 10.

possibly due to perturbation effects of the crystalline field or to small changes in hydrogen-bond distances. The additional bands in the 3000 cm.$^{-1}$ region may arise from combination of the OH stretching frequency with lattice vibrations or with low frequencies associated with the dimeric ring;[6] *e.g.*, in the spectrum of hexanoic acid these bands are at approximately constant frequency intervals of *ca.* 60 cm.$^{-1}$. An alternative explanation for the extra peaks may be in terms of summation bands due to appropriate combinations of fundamental vibrations of the coupled carboxyl groups of the dimeric molecules.[7]

TABLE 1.

	νC=O (cm.$^{-1}$)				νC=O (cm.$^{-1}$)		
Acid	liquid	crystalline	ν (cm.$^{-1}$)	Acid	liquid	crystalline	ν (cm.$^{-1}$)
Acetic	1715	1654	−61	Heptanoic ...	1724	1710	−14
Propionic ...	1725	1730, 1710 (sh)	+ 5?	Octanoic ...	1722	1702	−20
Butyric	1729	1740, 1705	+11?	Nonanoic ...	1726	1700	−26
Valeric	1722	1722	0	Decanoic ...	1716	1705	−11
Hexanoic ...	1721	1710	−11	Dodecanoic	1720	1705	−15

The band at 935 cm.$^{-1}$ increases in intensity on crystallisation whilst bands at 1435 and 1300 cm.$^{-1}$ become more intense and sharper. The band at 1435 cm.$^{-1}$ is almost absent in most of the liquid spectra.

X-Ray measurements on crystalline dodecanoic [8] and stearic acid [9] show that both exist in a dimeric form. Infrared measurements permit the deduction that most of the liquid acids also exist in the dimeric form. Hadži and Sheppard [10] have shown that, under these conditions, the dimeric carboxyl group gives rise to absorption bands at 1420 ± 20, 1300 ± 15, and 935 ± 15 cm.$^{-1}$. The first two bands correspond to closely coupled OH deformation and C–O stretching vibrations occurring in the plane of the $(CO_2H)_2$ dimeric ring; the third band is caused by the out-of-plane OH deformation vibration. As bands in these regions occur for all the liquid and solid monocarboxylic acids examined in the present investigation, it seems very probable that these acids also exist in the dimeric form in both the liquid and the solid state; however, formic acid exists as a polymer in both states.[11]

The bands in the solid-state spectra have been assigned to particular vibrations (although this is somewhat tentative in part, Fig. 3). Bands have been assigned to dimeric carboxyl vibrations following the asignments by Hadži and Sheppard.[10]

The bands at *ca.* 1435, 1300 ± 15, and 935 ± 15 cm.$^{-1}$ and a band near 680 cm.$^{-1}$ are thus assigned to dimeric carboxyl vibrations, the last being assigned to a $\delta C\lesssim^{O}_{O}$ angle deformation mode; a band occurring at *ca.* 1420 cm.$^{-1}$ is associated with a CH_2 group immediately adjacent to a carbonyl group,[12] and the remaining bands in the 1500—700 cm.$^{-1}$ region are tentatively assigned by analogy with similar classifications in hydrocarbons [13] and alkyl bromides.[14]

Two constant sets of bands at 1460 and 1380 cm.$^{-1}$ arise from CH_2 and CH_3 symmetric bending deformation modes respectively, and a variable set of bands at *ca.* 1450 cm.$^{-1}$ is probably due to CH_3 asymmetric bending modes. These are well-known frequencies and occur in the spectra of all paraffinic compounds. In alkyl bromides [14] a regular array of bands has been traced to its origin near 1250 cm.$^{-1}$ in the spectrum of the first member

[6] Davies and Evans, *J. Chem. Phys.*, 1952, **20**, 342.
[7] Bratoz, Hadži, and Sheppard, *Bull. sci. Conseil Acad. R.P.F., Yougoslavie*, 1953, **1**, 71.
[8] Vand, Morley, and Lomer, *Acta Cryst.*, 1951, **4**, 324.
[9] von Sydow, *ibid.*, 1955, **8**, 557.
[10] Hadži and Sheppard, *Proc. Roy. Soc.*, 1953, *A*, **216**, 247.
[11] Chapman, *J.*, 1956, 225.
[12] Francis, *J. Chem. Phys.*, 1951, **19**, 942.
[13] (*a*) Brown, Sheppard, and Simpson, *Discuss. Faraday Soc.*, 1950, **9**, 261; (*b*) *Phil. Trans. Roy. Soc.*, 1954, *A*, **247**, 35.
[14] Brown and Sheppard, *Trans. Faraday Soc.*, 1954, **50**, 535.

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of the series and shown to originate from CH_2 wagging vibrations. In the higher members frequencies split out from this origin towards higher and lower frequencies within the range 1200—1380 cm.$^{-1}$. In the monocarboxylic acids a similar distribution of frequencies occurs in this region. The origin of this distribution might be expected to occur in the spectrum of propionic acid and it is possible to trace a series of bands back to a band near 1250 cm.$^{-1}$ in this spectrum (see Fig. 3). Previously this band has been tentatively assigned to a dimeric carboxyl vibration [10] but the present assignment to a CH_2 wagging or twisting mode seems better, particularly since a band persists in this position even in the deuterated molecule. Whilst the analogy with the spectra of the alkyl bromides suggests that this distribution also arises from CH_2 wagging modes, this conclusion is not certain since no detailed assignment of dimeric propionic acid is yet available to show that the band at 1250 cm.$^{-1}$ arises from an in-plane vibration. Jones *et al.*[2] assign the distribution generally to CH_2 wagging and twisting modes.

A band at 1080 cm.$^{-1}$ in the spectrum of crystalline propionic acid is assigned to a methyl rocking mode. It may in fact correspond to both in-plane modes. The out-of-plane CH_3 rocking modes may give rise [14] to a band near 890 cm.$^{-1}$ but this region is covered by part of the absorption due to the (δOH) mode near 930 cm.$^{-1}$ and no significant series can be picked out. Series of bands in the 900—720 cm.$^{-1}$ region are attributed to CH_2

TABLE 2. *Frequencies (cm.$^{-1}$) assigned to* $\delta[CH_2]_n$ *rocking vibrations.*

n	Monocarboxylic acids, $H{\cdot}[CH_2]_n{\cdot}CO_2H$	Dicarboxylic acids, $HO_2C{\cdot}[CH_2]_n{\cdot}CO_2H$	Paraffins, $H{\cdot}[CH_2]_n{\cdot}H$
2	807	804	822
3	750	754	748
4	731	733	732
5	727	731	728
6	724	725	726
7	723	726	723
8	723	722	722
9	721	—	720
11	721	—	720

rocking modes. The most characteristic series of bands in the 720—810 cm.$^{-1}$ region is listed in Table 2 which also shows the corresponding CH_2 rocking frequencies for normal paraffins [13a] in the crystalline state and for the dicarboxylic acids.[15] Comparison of these data confirms our assignments. It also suggests that the acids which are liquid at room temperature crystallise predominantly in the same *trans*-zig-zag configuration as do the acids which are normally solid at room temperature.

APPENDIX

Possible New Polymorphic Forms of Decanoic Acid.—When the spectrum of decanoic acid is obtained at different temperatures, marked changes are observed (Fig. 4). The frequencies (cm.$^{-1}$) of some of the main bands at different temperatures are shown in Table 3.

TABLE 3.

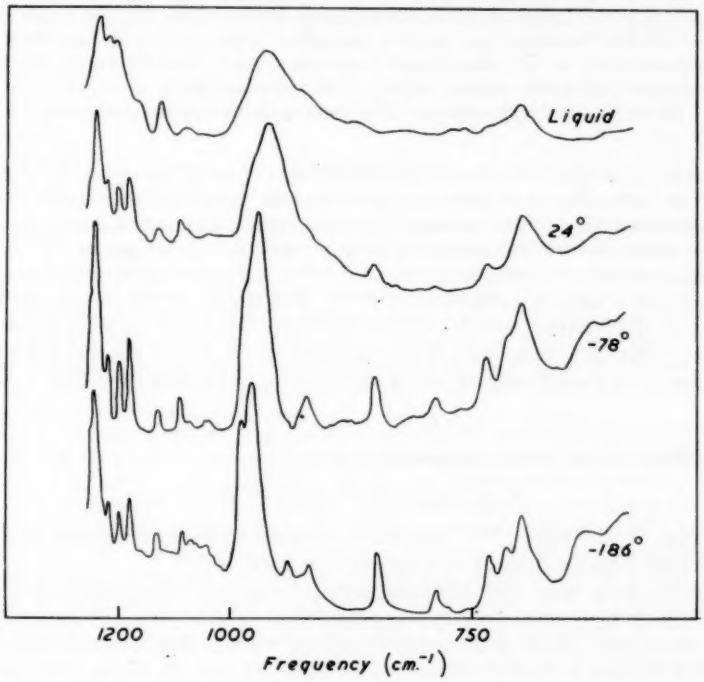
	$\nu C{=}O$	δ(OH)	$\delta C\lesssim^{O}_{O}$	δCH_2 rocking
Liquid	1714	937	—	720
Crystalline, 24°	1698	935	678	720
Crystalline, −78°	1700	946, 964 (sh)	687	729, 721
Crystalline, −186°	1700, 1692	957, 975 (sh)	690, 668	729, 721

The broad band assigned to the out-of-plane OH bending vibration shifts and narrows as the temperature is lowered. (This may be due to depopulation of dimeric ring vibrations of higher energy.) Further, between 24° and −78° the band at 720 cm.$^{-1}$ (assigned to a CH_2

[15] Corish and Davison, *J.*, 1955, 2431.

rocking mode) splits into two components (at 721 and 729 cm.$^{-1}$). The latter behaviour is analogous to the change observed [16] when long-chain hydrocarbons, esters, and alcohols change from a hexagonal form with rotating chains to a more stable form (probably with orthorhombic packed chains). This prompts the suggestion that a similar type of polymorphic change occurs for decanoic acid. (It would be of interest to study this phenomenon with nuclear magnetic resonance spectroscopy to see whether there is rotation of the chains, and also by *X*-rays to see whether a phase change has occurred.) It might, however, be argued that contraction of the

FIG. 4. *Spectrum of decanoic acid at various temperatures.*



lattice might also produce this change since it increases the opportunity for interaction between adjacent methylene chains (cf. Stein [17]).

Below −78°, further gradual shifts in the frequencies of the bands occur, in particular of the band assigned to the δOH out-of-plane vibration (see Table 3). At −186°, the absorption near 1700 cm.$^{-1}$ consists of two peaks. This is of interest since von Sydow reports that the absorption near 1700 cm.$^{-1}$ in the B-form of stearic acid consists of two close peaks despite the fact that crystals in this form do not contain two different C=O bonds. Since there are four molecules per unit cell in this crystal, coupling of the vibrations can occur, giving rise to a number of components of the fundamental vibrations. This might suggest a further polymorphic transition below −78° in decanoic acid, but this seems improbable. It may be that hydrogen bonding of the carboxyl groups of the dimer is sensitive to the lattice contraction.

Mr. C. G. Baker is thanked for experimental assistance to one of us (P. J. C.), and the Dunlop Rubber Co. Ltd. and Unilever Ltd. are thanked for permission to publish this work.

(P. J. C.) CHEMICAL RESEARCH DEPARTMENT, DUNLOP RESEARCH CENTRE, BIRMINGHAM, 24.
(D. C.) RESEARCH DEPARTMENT, UNILEVER LTD., PORT SUNLIGHT, CHESHIRE.

[*Received, August 1st,* 1956.]

[16] Chapman, Sixth Internat. Spectroscopic Symp., Amsterdam, 1956.
[17] Stein, *J. Chem. Phys.*, 1955, **23**, 734.

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331. *The Nature and Stability of the Complex Ions formed by Ter-, Quadri-, and Sexa-valent Plutonium Ions with Ethylenediaminetetra-acetic Acid. Part I.* pH *Titrations and Ion-exchange Studies.*

By J. K. Foreman and T. D. Smith.

Potentiometric pH titrations and cation-exchange studies have shown that plutonium(III), plutonium(IV), and plutonyl ions form 1 : 1 chelates with ethylenediaminetetra-acetic acid (edta). In the first two cases complexes containing two atoms of plutonium to one molecule of edta are also formed. The stability constants for the 1 : 1 complexes of the three ions have been determined by a cation-exchange technique; the values of log K are: plutonium(III), 18·12; plutonium(IV), 17·66; plutonyl, 16·39.

The value for the plutonium(IV) chelate relates to a hydrolysed species of the ion.

The properties of complex ions formed by the reaction of metal ions with chelating agents of the amino-carboxylic acid type in general, and ethylenediaminetetra-acetic acid (edta) in particular, have been studied by a variety of techniques, notably potentiometric pH titration,[1,2,3] oxidation–reduction titration,[4] polarography,[3,5] electrode-potential measurements,[6,7] spectrophotometry,[8,9,10] reaction rate kinetics,[11,12] and methods based on solubility, solvent extraction, etc.[13,14] The nature of the component ions and the stability of the resulting complex largely determined the most appropriate method of examination. The tetrabasic edta being denoted as H_4Y, its general reaction with plutonium ions over the pH range in which chelation can occur may be written

$$mPu^{a+} + nH_bY^{-4+b} = Pu_mY_n^{ma-4n} + nbH^+ \quad . \quad . \quad . \quad . \quad (1)$$

and the stability constant of the chelate is then given by

$$K_c = [Pu_mY_n^{ma-4n}]/[Pu^{a+}]^m[Y^{4-}]^n \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The evaluation of the term $[Y^{4-}]$ requires a knowledge of the ionisation constants of edta; these have been determined by a number of workers.[1,15,16]

This paper is concerned with the assignment of values to m, n, and K_c for the edta chelates of the ions of ter-, quadri- and sexa-valent plutonium. The formulæ of the complexes were derived from potentiometric pH titration of the hydrogen ions liberated on chelation according to equation (1).

The stability constants of the edta chelates of plutonium(III) and plutonium(IV) are likely to be high as judged purely from ionic charge density considerations and, in the case of plutonium(III), from the reported [3] high stabilities of the corresponding complexes of the formally analogous rare-earth metal ions. Hence, unless a competitive complex-forming technique of the type described by Schwarzenbach and Freitag [2] is employed, these stability constants cannot be accurately evaluated from pH titration curves by the

[1] Schwarzenbach and Ackermann, *Helv. Chim. Acta*, 1947, **30**, 1798.
[2] Schwarzenbach and Freitag, *ibid.*, 1951, **34**, 1503.
[3] Wheelwright, Spedding, and Schwarzenbach, *J. Amer. Chem. Soc.*, 1953, **75**, 4196.
[4] Schwarzenbach and Heller, *Helv. Chim. Acta*, 1951, **34**, 576.
[5] Kolthoff and Auerbach, *J. Amer. Chem. Soc.*, 1952, **74**, 1452.
[6] Bjerrum and Nielsen, *Acta Chem. Scand.*, 1948, **2**, 297.
[7] MacNevin and Kriege, *J. Amer. Chem. Soc.*, 1955, **77**, 6149.
[8] Plumb, Martell, and Bersworth, *J. Phys. Colloid Chem.*, 1950, **54**, 1208.
[9] Martell and Plumb, *J. Phys. Chem.*, 1952, **56**, 993.
[10] Hughes and Martell, *ibid.*, 1953, **57**, 694.
[11] Jones and Long, *ibid.*, 1952, **56**, 25.
[12] Cook and Long, *J. Amer. Chem. Soc.*, 1951, **73**, 4119.
[13] Irving and Williams, Proc. Internat. Analyt. Congress, Oxford, 1952, p. 257.
[14] Irving and Williams, *Nature*, 1948, **162**, 764.
[15] Carini and Martell, *J. Amer. Chem. Soc.*, 1952, **74**, 5745.
[16] Cabell, Atomic Energy Research Establishment Report A.E.R.E. C/R.813.

familiar Bjerrum [17] method. Accordingly, they have been determined by the cation-exchange procedure developed initially by Schubert,[18,19,20] which can be applied both when the resulting complex is a cation and is itself adsorbed by the cation-exchange resin,[21,22] and when the complex is neutral or anionic and does not undergo exchange. In the latter instance, provided the cation concentration is negligible compared with that of the chelating agent, the simple equation derived by Schubert may be applied in the form :

$$\log (\lambda_0/\lambda - 1) = \log K_c + x \log [Y^{4-}] \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where λ_0 and λ are the ion-exchange distribution coefficients respectively in the absence and the presence of a large excess of edta, and x is the number of edta ions bound per atom of plutonium. It will be shown from the pH titration curves that, for any excess of edta over plutonium, $x = 1$; hence the edta chelates of the three plutonium ions under consideration are anionic and equation (3) may be used to evaluate K_c.

Experimental

pH *Titrations.*—The technique employed was essentially similar to that of Cabell [16] for studying the reactions of uranyl and thorium ions with complexones. The titration apparatus comprised a 200 ml. beaker fitted with a rubber bung carrying the electrodes (glass and saturated calomel), a burette, stirrer, and inlet and outlet tubes for passage of nitrogen. The titrations were carried out by mixing solutions of plutonium and the dipotassium salt of edta in the required stoicheiometric proportions in constant ionic strength of 0·1N-potassium chloride and titrating against 0·05N-potassium hydroxide with use of an Electronic Instruments Direct Recording pH meter, all operations being performed in an atmosphere of nitrogen and at room temperature (20° ± 0·5°). The edta used in preparing the dipotassium salt was purified by Blaedel and Knight's method.[23]

Plutonium(III) solutions were prepared by dissolving the metal in 5N-hydrochloric acid. To remove the free hydrochloric acid without hydrolysing the plutonium trichloride the required volume was introduced into the titration vessel and evaporated to dryness in a current of nitrogen before addition of the chelating agent. Plutonium(IV) solutions were made by dissolving the hydroxide in 8N-nitric acid. Removal of excess of nitric acid in a stream of nitrogen led to erratic results, and consequently all titration curves were corrected for this free acidity which was determined by titration with sodium hydroxide after precipitation of the plutonium as ferrocyanide. Plutonium(VI) solutions were prepared by anodic oxidation of plutonium(IV) in dilute nitric acid, and their pH was adjusted to that of the dipotassium edta solution before titration. All plutonium(VI) solutions used were shown chromatographically [24] to contain less than 1% of plutonium(IV).

Ion-exchange Studies.—The pH dependence of the term $[Y^{4-}]$ introduces a similar dependence in the extent of chelate formation, and in order to carry out determinations over a wide range of $[Y^{4-}]$ values it is necessary to select a pH at which reasonable values of λ_0 and λ [equation (3)] are obtained over this range. Preliminary experiments indicated that pH 3·30 fulfilled this requirement. Strict control of pH throughout the experiments is essential; the use of buffer solutions for this purpose was not favoured since it introduced a (possibly unknown) correction for the competitive complex-formation by the weak acid anion of the buffer. Instead, unbuffered media were used and extreme care taken to condition the resin to pH 3·30 before use.

All solutions were made up in 0·1N-potassium chloride solution and were about 10^{-7}M in plutonium. The concentration range of chelating agent studied was 10^{-6}M to 10^{-4}M. 20 ml. of each solution were shaken mechanically for 12 hr. with 0·2 g. of 60—80-mesh Amberlite IR 120 cation-exchange resin conditioned with 0·1N-potassium chloride at pH 3·30, and the plutonium concentration in the solution was determined before and after equilibration by α-particle

[17] Bjerrum, " Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941.
[18] Schubert, *J. Phys. Colloid Chem.*, 1948, **52**, 340.
[19] Schubert and Richter, *ibid.*, p. 352.
[20] Schubert and Richter, *J. Amer. Chem. Soc.*, 1948, **70**, 4259.
[21] Fronaeus, *Acta Chem Scand.*, 1951, **5**, 389.
[22] Carleson and Irving, *J.*, 1954, 4390.
[23] Blaedel and Knight, *Analyt. Chem.*, 1954, **26**, 741.
[24] Cowan and Foreman, *Chem. and Ind.*, 1954, 1583.

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counting. Temperature variations were less than $\pm 0{\cdot}2°$ and occasional checks failed to reveal changes of greater than 0·01 pH unit.

The plutonium(III) solutions were made up in the presence of 0·003M-hydroxylamine hydrochloride and passed through a silver reductor immediately before use as a precaution against the oxidation of plutonium(III) to plutonium(IV) which is thermodynamically possible at pH 3·30.[25] In the case of plutonium(IV) a direct determination at this pH of λ_0 in the absence of edta is impossible owing to hydrolysis of the Pu^{4+} ion;[26] λ_0 was therefore calculated by solving equation (3) from pairs of edta concentrations. To minimise effects due to the hydrolysis of the Pu^{4+} ion in the chelation studies the plutonium(IV) was added to the edta-containing solution in a very small volume (0·01 ml.) of 1N-nitric acid, and any small pH adjustment made subsequently.

Results and Discussion

pH *Titrations.*—(a) *Plutonium* (III) *and plutonium*(IV). Figs. 1 and 2 show the titration curves for plutonium(III) and plutonium(IV); in each, the mole ratio of edta to plutonium was varied from 0·5 to 4. The curves for both ions are very similar and in no case did any precipitation occur up to the highest pH values recorded. Curves *C*, *D*, and *E* demonstrate that the only inflexion which occurs is at pH 4 approximately where two moles of alkali per mole of plutonium have been added, which corresponds to the formation of 1 : 1 chelates according to the equations

$$Pu^{3+} + H_2Y^{2-} = PuY^- + 2H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and

$$Pu^{4+} + H_2Y^{2-} = PuY + 2H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The latter equation should more strictly be represented as

$$Pu(OH)_n^{4-n} + H_2Y^{2-} = Pu(OH)_nY^{n-} + 2H^+ \quad . \quad . \quad . \quad (5a)$$

to allow for the hydrolysis of the plutonium(IV) ion.

The inflexion is complete at about pH 5, though clearly the chelates can exist, at least partially, at considerably lower pH values, the lower limit for complex formation being governed directly by the stability of the appropriate complexes. Above pH 5 the titration curves rise less steeply than predicted theoretically, and this is presumably due to the liberation of further quantities of hydrogen ion by hydrolysis of the complexes. This can be most simply represented in stages such as

$$PuY^- + H_2O = PuY(OH)^{2-} + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

and similarly for plutonium(IV).

The addition of a second ligand through the partially dissociated species of edta does not occur when excess of chelating agent is present. At the higher pH values the curves are adequately represented by the third neutralisation of the excess of edta, except that the neutralisation point is shifted to larger titres by the hydrolysis of the complex. However, the addition of Y^{4-} ions to the complex at high pH cannot be ruled out since no hydrogen ion is involved and the titration curve would be unaffected.

The absence of precipitation in the titration of the solution containing a twofold excess of plutonium to edta (Curve B, Figs. 1 and 2) indicates the formation of stable complexes. These complexes are of the type Pu_2Y, since titrations carried out with larger excesses of plutonium to edta yielded hydroxide precipitates. Formation of stable complexes according the equations [which neglect hydrolysis of plutonium(IV)]

$$Pu^{3+} + \tfrac{1}{2}H_2Y^{2-} = \tfrac{1}{2}Pu_2Y^{2+} + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

and

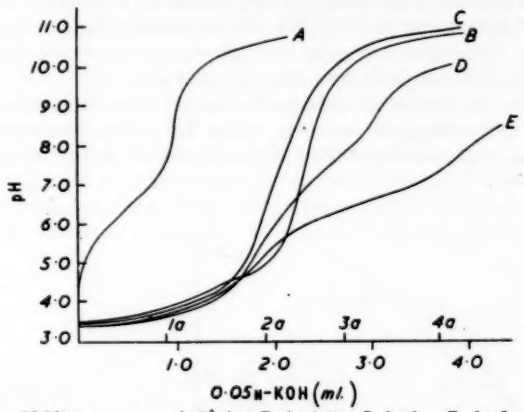
$$Pu^{4+} + \tfrac{1}{2}H_2Y^{2-} = \tfrac{1}{2}Pu_2Y^{4+} + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

should lead to inflexions at the addition of one mole of alkali per mole of plutonium, and it must be assumed that hydrolysis of the complexes to $Pu_2Y(OH)_2$ and $Pu_2Y(OH)_2^{2+}$ occurs

[25] "The Transuranium Elements" (Ed. Seaborg, Katz, and Manning), National Nuclear Energy Series, IV–14B, Part 1, McGraw-Hill, London, 1949, p. 253.
[26] Kraus and Nelson, *J. Amer. Chem. Soc.*, 1950, **72**, 3901.

at low pH in order to account for the observed inflexion at two moles of alkali per mole of plutonium. The existence of Pu_2Y-type complexes for plutonium(III) and plutonium(IV) accords with Cabell's observation [16] of the formation of similar complexes of thorium and uranium(VI), the latter being unstable. Schwarzenbach, Ackermann, and Ruckstuhl [27] have noted similar species, and measured the relevant equilibrium constants, between calcium and magnesium ions and 1 : 3- and 1 : 4-diamino*cyclo*hexane-*NNN'N'*-tetra-acetic acid.

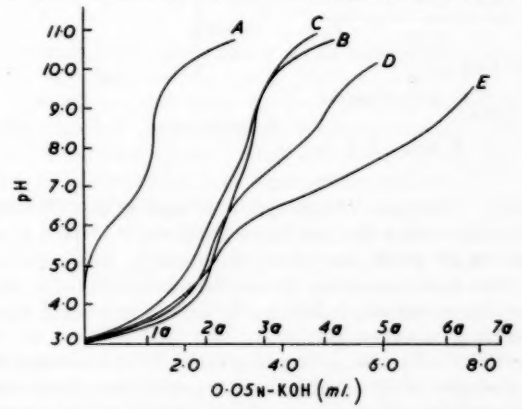
FIG. 1. pH *Titration of the plutonium*(III)*–edta system.*



Ratio Pu : H_2Y^{2-} ..... *A*, 0 : 1; *B*, 1 : 0·5; *C*, 1 : 1; *D*, 1 : 2; *E*, 1 : 4.

The numerals followed by *a* in this and other Figures give the number of equivalents of alkali per mole of plutonium.

FIG. 2. pH *Titrations of the plutonium*(IV)*–edta system* (*key as in Fig.* 1).



Above a pH of about 3·5 the edta complexes of plutonium(III) are thermodynamically unstable with respect to those of plutonium(IV), since then plutonium(III) is oxidised by water to plutonium(IV).[25] Uncomplexed plutonium(III) becomes oxidised to plutonium(IV) and can undergo exchange with complexed plutonium(III) ions. The extent of this interconversion will depend upon the rate of exchange between free and complexed plutonium ions, and upon the concentration of free plutonium ions. The former quantity may not be negligible since the complexes are essentially ionic, but the latter is extremely

[27] Schwarzenbach, Ackermann, and Ruckstuhl, *Helv. Chim. Acta*, 1949, **32**, 1175.

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small and ever decreasing above pH 3·5 on account of the high stability of the complexes. In addition, it is probable that the plutonium(IV) content of the uncomplexed plutonium at such pH values would be appreciably colloidal as a result of hydrolysis.[26] Thus the overall interconversion process is likely to be a slow one, and this is qualitatively verified by the colour differences in solutions of the plutonium(III) and plutonium(IV) chelates on completion of the potentiometric titrations.

Plutonium(VI). The titration curves for the plutonium(VI)–edta system are reproduced in Fig. 3. In these titrations no precipitation occurred up to the maximum pH values studied, indicating the presence of a stable 1 : 1 complex. In the case of the uranyl ion Cabell [16] finds a complex UO_2HY^+ which is unstable, precipitation occurring in the region of pH 8. This difference may be attributed to the much reduced tendency for the plutonyl than for the uranyl ion to undergo hydrolysis.

There appear to be no stable plutonyl–edta chelates containing more than one molar equivalent of plutonium to edta, since titrations performed with solutions containing an excess of plutonium yielded indefinite curves and a plutonate precipitate at pH 10 approximately.

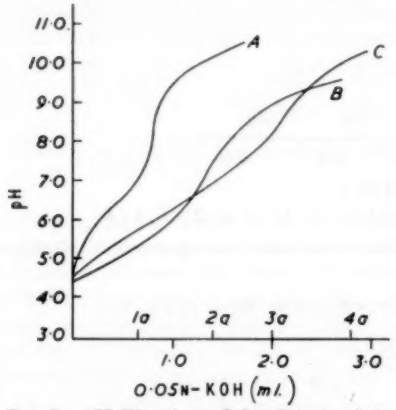

FIG. 3. pH *Titrations of the plutonium*(VI)–*edta system.*

Ratio Pu(VI) : H_2Y^{2-} ... *A*, 0 : 1; *B*, 1 : 1; *C*, 1 : 2.

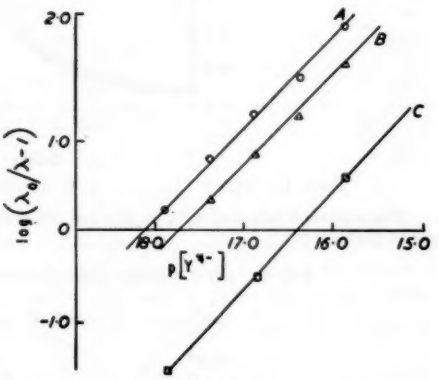

FIG. 4.

A, Pu(III)–edta. *B*, Pu(IV)–edta. *C*, Pu(VI)–edta.

Ion-exchange results. The plots of log $(\lambda_0/\lambda - 1)$ against log $[Y^{4-}]$ are shown in Fig. 4. It is evident from the slopes that the complexes are of the 1 : 1 type in each instance, and the log K_c values are 18·12, 17·66, and 16·39, respectively, for plutonium-(III), -(IV), and -(VI). It is unlikely that these values are in error by more than $\pm 3\%$ except in the case of plutonium(IV), where the calculated values for λ_0 showed an overall spread of about 10% and the total error in log K_c could be $\pm 5\%$.

The Stability Constants.—In attempting to correlate the measured stability constants for the plutonium chelates of edta with those reported for other elements it must be remembered that the stability constant is not itself a fundamental quantity, but is related to the entropy and enthalpy of the system. For thermodynamic stability constants the relation assumes the familiar form

$$-RT \ln K_a = \Delta G^\circ = \Delta H^\circ - T\Delta S^\circ \quad . \quad . \quad . \quad . \quad . \quad (9)$$

For chelates of high stability the entropy term becomes predominant, as demonstrated by Carini and Martell [28] and by Charles.[29] Of the factors contributing to the increase in

[28] Carini and Martell, *J. Amer. Chem. Soc.*, 1954, **76**, 2153.
[29] Charles, *ibid.*, p. 5854.

entropy on chelate formation the most important is the increase in the number of particles in the system arising from the release of water molecules from the hydrated cation to the bulk solution. This entropy increase, shown to be 16·7 e.u. per water molecule,[30] can therefore be considerable in the formation of edta chelates assuming that one water molecule is released for each bond formed by the ligand, though it is partially offset by the entropy decrease, calculated by Cobble[31] to be 14 e.u. for each ring formed. Where similar elements form chelates of high stability with a particular ligand the value of the partial molal entropy of the ions concerned should provide a relative guide to the stability constants of the chelates. The rare-earth elements, and possibly the actinides, are probably the only series of ions having the required degree of similarity in charge and radius necessary to maintain the entropy and enthalpy changes on chelate formation sufficiently constant to test this approach. Fig. 5 shows the plot of log K for the edta chelates against partial molal entropy of the lanthanide ions above gadolinium, where the chelates are considered[3] to be isostructural. The graph is reasonably linear in view of experimental errors involved in determination of the stability constants and some uncertainty regarding the values of the ionic radii used in evaluating the partial molal entropies.[3]

Apart from the value reported above for plutonium(III), no data are available for the edta chelates of the actinide elements. However, from the similarity in charge and

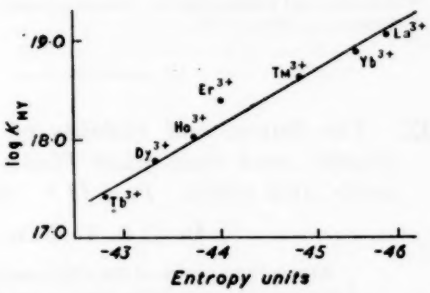

FIG. 5. *Stability constant–entropy relation for reaction* $M^{3+} + Y^{4-} \rightleftharpoons MY^{1-}$.

entropy between elements in the two series it seems unlikely that the log K values for the edta chelates of the actinides will be much displaced from those of the corresponding lanthanides, and the experimental value for plutonium(III) supports this view. Whilst such correlations hold strictly only for thermodynamic stability constants, it is apparent from the work of Martell and Carini[28] that errors introduced in using concentration stability constants are small provided that these are determined at fairly low ionic strength.

The partial molal entropy of the Pu^{4+} ion (−87 e.u.)[32] is more negative than the values for Fe^{3+} (−70·1 e.u.)[32] and Cr^{3+} (−73·5 e.u.),[32] both of which form very stable complexes with edta, *e.g.*, log $K = 25·0$ for the iron(III) complex. This, together with the analogous case of thorium (log $K = 23·2$),[33] suggests that the log K value of 17·7 for plutonium(IV) is anomalously low. However, at pH 3·30, at which the determinations were performed, hydrolytic effects will be such that the concentration of Pu^{4+} will be negligible and the major species present will be the first hydrolysis product $Pu(OH)^{3+}$. The experimental conditions are, in fact, sufficient to permit further hydrolysis to the irreversible stages of the mechanism, but it would appear from the experimental results that the presence of the chelating agent, together with the hydrolysis-minimising method of introducing the plutonium(IV) into the system, has largely prevented this. Whilst the partial molal entropy of the ion $Pu(OH)^{3+}$ is not recorded, this property is very similar for the ions U^{3+} and $U(OH)^{3+}$,[32] and the value for Pu^{3+} being taken as a first approximation for that of

[30] Latimer, "Oxidation Potentials," 2nd Ed., Prentice-Hall, New York, 1952, p. 39.
[31] Cobble, *J. Chem. Phys.*, 1953, **21**, 1451.
[32] *Op. cit.*, ref. 30, p. 298.
[33] Schwarzenbach, *Analyst*, 1955, **80**, 713.

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$Pu(OH)^{3+}$, the similar observed stability constants for the edta chelates of plutonium(III) and plutonium(IV) at pH 3·30 may be understood.

Experimental confirmation that at pH 3·30 the plutonium(IV) chelate should be formulated as a negatively charged species, say $PuY(OH)^-$, rather than PuY, is forthcoming from the appreciable adsorption of the chelate at this pH on the anion-exchange resin Amberlite IRA-400. This behaviour is consistent with the hydrolysis of the Pu^{4+} ion, rather than formation of the complex PuY and its subsequent hydrolysis, since from the pH titration curves the latter effect is negligible at pH 3·30. Again, spectrophotometric examination of the plutonium(IV)–edta system in 1N-nitric acid indicates a log K of about 24·2 for the unhydrolysed Pu^{4+} ion chelate.[34]

The relatively high stability of the plutonyl chelate of edta contrasts markedly with that of the uranyl ion which forms only a very weak complex. Hydrolysis and polymerisation of the uranyl ion [35] at low pH to give ions of charge density too low for stable chelate formation account for this difference.

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WINDSCALE WORKS, SELLAFIELD, CUMBERLAND. [*Received, August 24th,* 1956.]

[34] Foreman and Smith, Part II, following paper.
[35] Sutton, *J.*, 1949, S 275.

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332. *The Nature and Stability of the Complex Ions formed by Ter-, Quadri-, and Sexa-valent Plutonium Ions with Ethylenediaminetetra-acetic Acid (edta). Part II.* Spectrophotometric Studies.*

By J. K. FOREMAN and T. D. SMITH.

Absorption spectra of the ethylenediaminetetra-acetates of plutonium(III), plutonium(IV), and plutonium(VI) are presented, and the stability constants of these chelates obtained from them. Chelation of the unhydrolysed plutonium(IV) ion with ethylenediaminetetra-acetate in 1N-nitric acid has been observed.

SEVERAL attempts have been made to correlate shifts in absorption spectra which occur on chelate formation with structure, bond-type, and stability of the chelates. Martell and his co-workers [1-3] have examined the spectra of a number of edta chelates and given orders of relative stabilities [4] for a number of elements at pH values in the range 4·00—11·00; for essentially ionic chelates, the edta absorption band shifts to progressively shorter wavelengths with increasing stability of the chelates.

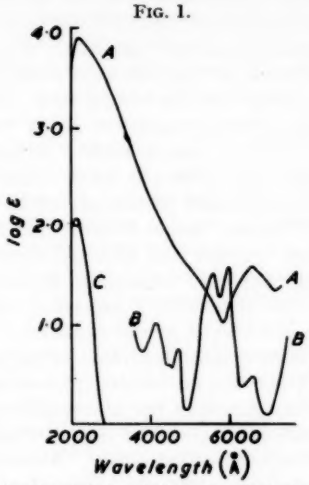
The absorption spectra of the edta chelates of plutonium have been recorded primarily to obtain confirmatory values for the chelate stability constants reported in Part I.* The spectra of the fully formed complexes are plotted in Figs. 1, 2, and 3 together with the spectra of the component ions.

The spectra of the 1 : 1 complexes of plutonium(III) and plutonium(IV) are markedly different from those of the unchelated ions; not only is there considerable intensification of the spectrum, but several peaks characteristic of the aqueous ions are either missing or

* Part I, preceding paper.

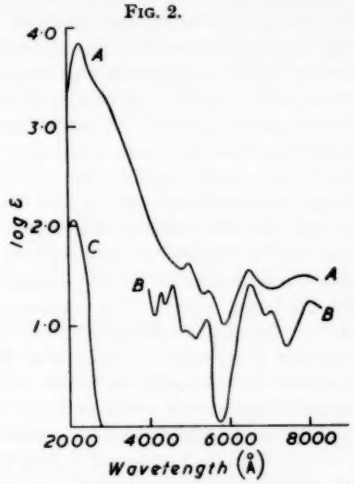
[1] Martell and Calvin, "Chemistry of the Metal Chelate Compounds," Prentice-Hall Inc., New York, 1952.
[2] Hughes and Martell, *J. Phys. Chem.*, 1953, **57**, 694.
[3] Martell and Plumb, *ibid.*, 1952, **56**, 993.
[4] Plumb, Martell, and Bersworth, *J. Phys. Colloid Chem.*, 1950, **54**, 1208.

FIG. 1.



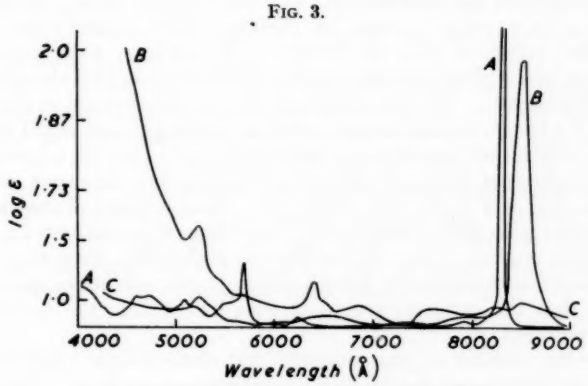
A, 1 : 1 edta chelate of plutonium(III) at pH 4·7.
B, Unchelated plutonium(III) at pH 1·0.
C, Tetrasodium salt of edta at pH 10·0.

FIG. 2.



A, 1 : 1 edta chelate of plutonium(IV) at pH 4·7.
B, Unchelated plutonium(IV) at pH 1·0.
C, Tetrasodium salt of edta at pH 10·0.

FIG. 3.



A, Unchelated plutonyl ion in 0·1N-nitric acid.
B, ,, ,, at pH 6·5.
C, 1 : 1 edta complex of plutonyl ion at pH 6·5.

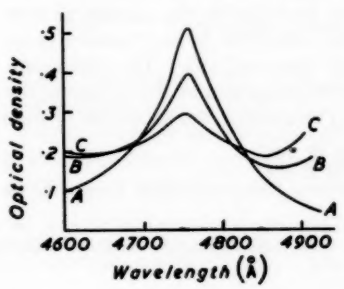


FIG. 4.

$1{\cdot}63 \times 10^{-3}$M-Plutonium(IV) in :

A, N-Nitric acid.
B, N-Nitric acid + $1{\cdot}63 \times 10^{-3}$M-edta.
C, ,, + $3{\cdot}26 \times 10^{-3}$M-edta.

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have undergone wavelength displacement. The general intensification of the absorption spectrum accords with the findings of Moeller and his co-workers [5,6] for the edta chelate of neodymium and the acetylacetone complexes of several rare-earth elements, where the effect is attributed to enhancement of electronic $4f^n$ transitions, forbidden for the free atoms, due to the increased electric dipole arising from the strong field imposed by the chelating anions. It seems likely that a similar effect is operative in the case of plutonium(III) and plutonium(IV) since considerable evidence is now available [7] suggesting that the absorption spectra of the actinide elements arise from electronic transitions between terms of the $5f^n$ series. The spectrum of unchelated plutonium(III) in 0·1M-potassium chloride solution undergoes virtually no intensity changes between pH 1 and the pH used to record the spectrum of the fully formed complex (pH 4·7), and the entire observed intensification of absorption on addition of edta may reasonably be ascribed to the chelating effect. For plutonium(IV), results quoted in Part I indicated that at pH 4·7 a partially hydrolysed species of the Pu^{4+} ion is involved in the chelation. It is known that progressive hydrolysis of this ion results in increased absorption of radiation, particularly at wavelengths below about 4500 Å.[8] Thus, the unchelated plutonium(IV) spectrum taken at pH 1·0 is probably not a true representation of the absorption due to the species undergoing chelation, and the true intensification observed due to chelation may be less than that observed in Fig. 2, especially at the lower wavelengths. Absorbancy measurements on plutonium(IV) solutions in which hydrolysis of the ion is prevalent tend to be variable owing to contributions from scattering resulting from polymerisation and ultimate formation of colloidal species.

The spectrum of the plutonyl–edta chelate (Fig. 3) shows virtually none of the features characteristic of the plutonyl ion; in particular, the strong absorption at 8320 Å is absent and a new peak appears at 5700 Å. [The characteristic absorption of plutonium(V) also occurs at this wavelength.] In contrast with plutonium(III) and plutonium(IV), the plutonyl chelate does not exhibit the pronounced absorption in the low-wavelength visible region. The absorption due to the plutonyl ion in this region is seen to be small at pH 1 but increases markedly with increasing pH, and at pH 6·5, at which the spectrum of the fully formed complex was taken, it is very large. It is noteworthy that the spectrum of the plutonyl chelate is the same whether the formation of the chelate is approached from acid or from alkaline conditions. If the increase in absorption due to the plutonyl ion in the region 4000—5000 Å with increasing pH is attributed to the formation of ionic hydrolysis products,[9] *e.g.*, $PuO_2(OH)^+$ or $PuO_2(OH)_2$, then the absence of this strong absorption when the chelate is formed under alkaline conditions and the pH brought to 6·5 suggests that the carboxyl groups of edta can replace the hydroxyl groups of the hydrolysed plutonyl ion.

Unlike the edta chelates of plutonium(III) and plutonium(IV), that of the plutonyl ion is unstable and decomposes slowly during a period of several days. The effects observed are a gradual increase in pH (from 6·5 to 8·1 in three days, and to 9·1 in six days), the reduction of plutonium(VI) to plutonium(IV), and a gradual change in colour from the original violet-blue of the chelate to pale yellow. The main absorption spectra changes are the decrease in intensity of the characteristic peak due to the chelate at 5700 Å, and the appearance of new absorptions at 4400, 5050, and 5550 Å, and broader peaks around 6500 and 8000 Å, all increasing in intensity with time and pH. The plutonium valency states present after a given period of standing were recognised by decomposing the chelate, making the solution about 2N in nitric acid, and examining the spectrum of the resulting

[5] Moeller and Brantley, *J. Amer. Chem. Soc.*, 1950, **72**, 5447.
[6] Moeller and Ulrich, *J. Inorg. Nuclear Chem.*, 1956, **2**, 164.
[7] "The Actinide Elements" (Ed. Seaborg and Katz), National Nuclear Energy Series IV-14A, McGraw-Hill, London, 1954, pp. 783 *et seq.*
[8] Ockenden and Welch, *J.*, 1956, 3358.
[9] "The Transuranium Elements" (Ed. Seaborg, Katz, and Manning), National Nuclear Energy Series IV-14B, Part I, McGraw-Hill, London, 1949, p. 528.

solution. After a solution of the plutonyl chelate had stood for six days, the spectrum showed clearly the presence of both plutonium(IV) (absorption peaks at 4500, 4760, 4950, 5450, 6600, 7960 Å) and plutonium(VI) (peak at 8320 Å). The mechanism of the reduction of the plutonyl chelate is not understood. Kraus and Dam [1] have observed self-reduction of plutonium(VI) at high pH, and it is possible that the presence of the electron-donating edta carbonyl groups around the plutonyl ion at pH 6·5 simulates high pH conditions of the unchelated ion.

Determination of Stability Constants.—The stability constant of the 1 : 1 chelate of plutonium(III) was determined directly by making optical-density measurements on a solution containing equimolar amounts of the component ions, and brought to pH 1·5 to produce appreciable decomposition of the chelate. The stability constant was evaluated by using measured molar absorbancies of the chelate and the uncomplexed ion and Cabell's values [10] for the ionisation constants of edta.

As indicated above, the spectra of the ions of plutonium(IV) and plutonium(VI) and of the plutonyl chelate are pH dependent. Isohydric conditions are therefore desirable for evaluating the required molar absorbancies needed to calculate the stability constants of the plutonium(IV) and plutonyl chelates, and to meet this condition the replacement method of Hughes and Martell [2] was employed, cadmium being used as the reference ion. Relative stability constants are evaluated according to

$$K = [\mathrm{Pu(IV)Y}][\mathrm{Cd^{2+}}]/[\mathrm{CdY^{2-}}][\mathrm{Pu(IV)^{4+}}]$$

where $K = K_{\mathrm{Pu(IV)Y}}/K_{\mathrm{CdY^{4+}}}$, and similarly for the plutonyl ion. Schwarzenbach's weighted value $\log K = 16{\cdot}1$ has been used for the stability constant of the cadmium chelate.[11] Table 1 lists the values obtained together with those from the ion-exchange technique. For each valency state the ion-exchange and spectrophotometric values for $\log K$ are in reasonable agreement.

Chelation of the Unhydrolysed Pu^{4+} *Ion.*—The low value for the stability constant of the plutonium(IV)–edta chelate has been attributed to the fact that the recorded value at pH 3·30 applies to a hydrolysed species of the Pu^{4+} ion. Assuming, by analogy with thorium, that an edta chelate of unhydrolysed Pu^{4+} would have $\log K = 23$ approximately, we may readily calculate that appreciable complex formation should occur in 1N-acid solutions. In 1N-acid it is considered that hydrolysis products of the Pu^{4+} ion are virtually non-existent and therefore any interaction observed between edta and plutonium(IV) must be attributed to chelation of the unhydrolysed ion, and would be the result of formation of a chelate of stability much greater than $\log K = 17{\cdot}66$ observed for

TABLE 1.

Ion	Method	pH	$\log K$
Pu(III)	Ion exchange	3·30	18·12
Pu(III)	Direct spectrophotometric	1·5	18·59
Pu(IV)	Ion exchange	3·30	17·66
Pu(IV)	Replacement spectrophotometry	3·30	17·10
Pu(VI)	Ion exchange	3·30	16·39
Pu(VI)	Replacement spectrophotometry	4·0	16·03

the interaction at pH 3·30. Fig. 4 shows the effect of edta addition upon part of the spectrum of plutonium(IV) in 1N-nitric acid, and it is evident that chelation is occurring. It is not possible to obtain an accurate value for the stability constant of the complex since its spectrum is not known and cannot be isolated. However, it is apparent from the spectra of the edta chelates of the plutonyl ion and of uranium(IV) [12] that hydrolysis

[10] Cabell, Atomic Energy Research Establishment Report AERE C/R813.
[11] Schwarzenbach, *Analyst*, 1955, **80**, 713.
[12] Smith, unpublished work.

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of the component cation mainly affects the absorption in the low-wavelength visible region and at higher wavelengths it is virtually unaffected. Thus, using molecular absorbancy values for the chelate of the hydrolysed plutonium(IV) ion at wavelengths of about 5000 Å and above, we can obtain a first approximation to the stability constant. By using 4900, 5600, and 5700 Å for ratios of edta to plutonium of 1 : 1, 2 : 1, and 3 : 1, mean values for log K of 24·2, 24·2, and 24·3 were obtained. Subject to the inaccuracies mentioned above, these values are clearly of the right order for the 1 : 1 chelate of a quadrivalent ion.

Experimental

All spectra were taken with a Hilger Uvispek spectrophotometer, both quartz and glass prisms and cells being used. Solutions of plutonium-(III), -(IV), and -(VI) were prepared as described in the previous paper and were used at concentrations of 0·7—3·0 × 10^{-2}M. Constant ionic strength of 0·1N-potassium nitrate or chloride was maintained.

Table 2.

Species	pH	λ (Å)	ε	Species	pH	λ (Å)	ε
Pu(IV)	3·30	5400	11·7	Cd–edta	3·30	5400	3·7
,,	,,	5500	11·4	,,	,,	5500	3·7
,,	,,	5600	11·9	,,	,,	5600	3·7
,,	,,	5700	11·9	,,	,,	5700	3·1
Pu(IV)–edta	,,	5400	51·4	PuO_2^{2+}	4·0	8600	3·9
,,	,,	5500	52·6	,,	,,	8700	0·6
,,	,,	5600	51·4	,,	,,	8800	0·3
,,	,,	5700	45·9	PuO_2^{2+}–edta	,,	8600	9·4
				,,	,,	8700	8·6
				,,	,,	8800	7·0

The stability constant of the plutonium(III) chelate was calculated from optical density measurements at 4200 Å and 5500 Å. At these wavelengths the edta ions do not contribute to the absorption. Adherence to Beer's law was established for both the chelate and the free Pu^{3+} ion.

For the replacement reactions used to determine the stability constants of the plutonium(IV) and plutonyl chelates, the wavelengths used and molar absorbancies of the relevant species are listed in Table 2. The cadmium ion has no absorption in the visible region. Replacement of plutonium(IV) at pH 3·30 fairly certainly results in the formation of colloidal species of this ion, and the data of Ockenden and Welch [8] have been used for the molar absorbancy of such species. For the plutonyl chelate pH 4·00 was chosen to yield a measurable amount of the species involved.

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Windscale Works, Sellafield, Cumberland. [*Received, August 24th*, 1956.]

333. *Exchange Studies of Certain Chelate Compounds of the Transitional Metals. Part II.* The Rate of Racemisation and Dissociation of the Tris-(1 : 10-phenanthroline)nickel(II) Ion.*

By R. G. Wilkins and M. J. G. Williams.

The exchange of phenanthroline between the tris-(1 : 10-phenanthroline)-nickel(II) ion ($[Ni\ phen_3]^{2+}$) and uncomplexed ligand has been studied in various solvents by using [^{14}C]phenanthroline. The simple rate law: R (the exchange rate, min.$^{-1}$ mole l.$^{-1}$) $= k[Ni\ phen_3]$† where k, the exchange rate constant $= 1{\cdot}6 \times 10^{15} \exp(-25{,}200/RT)$, is obeyed in aqueous solution at pH 5·7—11·7. Comparison with the racemisation rate constant already measured by others and now confirmed [$k = 1{\cdot}2 \times 10^{15} \exp(-24{,}900/RT)$ min.$^{-1}$] shows that the dissociation mechanisms of exchange and racemisation of $[Ni\ phen_3]^{2+}$ are identical. This involves the complete rupture of one phenanthroline–ligand bond and the subsequent rapid racemisation of the dissociated fragment.

This dissociative path for racemisation persists in alkaline solution (pH ~13) and in solutions in methanol–water, ethanol–water, ethanol, and nitrobenzene, despite a wide variation in rates in these solvents. These results confirm and amplify the conclusions already reached for aqueous acid solution.

There has been an increasing interest recently in the reactions of metal complexes of 1 : 10-phenanthroline (phen), 2 : 2′-dipyridyl (dipy), and related compounds.[1] Nickel and iron, amongst other metals, form with the bidentate ligands complex ions of general formula $[MA_3]^{n+}$. These have been resolved into enantiomorphs, which racemise at rates and in conditions suitable for study of the process.

Basolo, Hayes, and Neumann [2] investigated the rates of acid dissociation and the accompanying racemisation of tris-(1 : 10-phenanthroline)nickel(II) ion, $[Ni\ phen_3]^{2+}$, and found that, within experimental error, these two rates were the same. A similar result was obtained for the tris-(2 : 2′-dipyridyl)nickel(II) ion, $[Ni\ dipy_3]^{2+}$. Independently Davies and Dwyer [3] came to a similar conclusion for the reaction between $[Ni\ phen_3]^{2+}$ and ferrous ion. There seems little doubt that for these two nickel complexes a dissociative mechanism can completely account for the racemisation in the experimental conditions. It would be interesting therefore to extend this work to neutral and alkaline aqueous solutions as well as to non-aqueous solvents. The rates of dissociation of metal ammine complexes can be markedly affected by pH changes [4] so that a change in the mechanism of racemisation might appear in neutral or alkaline solution. Although this does not appear very likely with the $[Ni\ phen_3]^{2+}$ ion whose racemisation rate is almost pH-independent, it remains a real possibility with the $[Ni\ dipy_3]^{2+}$ ion which racemises more slowly in neutral than in alkali [5] or in acid [6,2] media. Davies and Dwyer [7] have measured the racemisation rates of $[Ni\ phen_3]^{2+}$ and $[Ni\ dipy_3]^{2+}$ in non-aqueous solvents, including alcohols, acetone, pyridine, and nitrobenzene, and suggest from the similarity of the energy of activation and PZ-factor that in these solutions, in contrast to water, an intramolecular mechanism

* Part I, *J.*, 1955, 4098.

† In this and similar equations the usual enclosing brackets of the complex ion have been omitted to avoid confusion with those indicating molar concentrations.

[1] Brandt, Dwyer, and Gyarfas, *Chem. Rev.*, 1954, **54**, 959.
[2] Basolo, Hayes, and Neumann, *J. Amer. Chem. Soc.*, 1953, **75**, 5102.
[3] Reported by Davies, *Rev. Pure Appl. Chem.* (*Australia*), 1954, **4**, 66.
[4] Popplewell and Wilkins, *J.*, 1955, 4098.
[5] Davies and Dwyer, *Trans. Faraday Soc.*, 1952, **48**, 244.
[6] Schweitzer and Lee, *J. Phys. Chem.*, 1952, **56**, 195.
[7] Davies and Dwyer, *Trans. Faraday Soc.*, 1954, **50**, 1325.

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operates. Indeed some preliminary work by Neumann [8] suggested that in water containing 0·7 mole-fraction of methanol, $[Ni\ phen_3]^{2+}$ racemised more rapidly than it dissociated. An intramolecular racemisation has been definitely established for the analogous iron(II) [9, 10] and iron(III) [11] complexes of dipyridyl and phenanthroline.

Dissociation rates of complex ions can be simply measured by isotopic ligand exchange. Provided that any direct bimolecular exchange path involving the ligand can be allowed for, the ligand-exchange rate provides a measure of the rate of the dissociation of the first ligand. Since in exchange no net reaction occurs, the nature of the intermediate species which may be present during acid dissociation need not be considered. This is particularly useful in non-aqueous solvents. Some qualitative studies of the $[Ni\ dipy_3]^{2+}$–Ni^{*2+} exchange have been reported [12] but quantitative metal–complex-ion exchanges have attendant difficulties absent from ligand-exchange work.[13] We have therefore synthesised [^{14}C]-phenanthroline and -dipyridyl [14] and now describe in detail the exchange between phenanthroline and the $[Ni\ phen_3]^{2+}$ ion in water (over a wide pH range) and, in less detail, that in ethanol, ethanol–water, methanol–water, and nitrobenzene. We conclude that, despite a wide variation in the racemisation rates in these solvents, $[Ni\ phen_3]^{2+}$ racemises by a dissociative mechanism (involving *complete* removal of one phenanthroline ligand) under all the conditions which we have used.

Experimental

Materials.—[^{14}C]Phenanthroline hydrate was prepared by a Skraup reaction with [1-^{14}C]-glycerol as described elsewhere.[14] Drying *in vacuo* over phosphoric oxide for about 24 hr. gave anhydrous [^{14}C]phenanthroline which was used in the non-aqueous solvent experiments. Hydrated $[Ni\ phen_3](NO_3)_2$ containing [^{14}C]phenanthroline was prepared from hydrated nickel nitrate (1 mole) and [^{14}C]phenanthroline (3·5 moles).[14] After recrystallising several times from small amounts of water the complex was dehydrated by heating at 80° for a few hr. *in vacuo* over phosphoric oxide in an Abderhalden drying pistol (Found: Ni, 8·15; 8·2. Calc. for $C_{36}H_{24}O_6N_8Ni$: Ni, 8·1%). The spectrum of an aqueous solution of this material agreed with that previously reported (*e.g.*, ref. 2). Both materials could be diluted about twenty times with inactive material to obtain activities suitable for most of the work. In a few experiments, exchange was initiated by injection of the original material into a system combining inactive materials. Inactive tris-(1 : 10-phenanthroline)nickel(II) nitrate, perchlorate, and iodide were prepared by standard methods. When available, " AnalaR " chemicals were used.

In earlier experiments optically active $[Ni\ phen_3](NO_3)_2$ was required in order to reproduce exactly the exchange conditions. Treatment of the racemate with aqueous potassium antimonyl (+)-tartrate precipitated (+)-[Ni phen$_3$]antimonyl (+)-tartrate.[15] This was filtered and the filtrate containing (−)[Ni phen$_3$]antimonyl (+)-tartrate freeze-dried. Acetone extracted from the residue (−)$[Ni\ phen_3](NO_3)_2$, $[\alpha]_D$ −1461°. Optically active anhydrous $[Ni\ phen_3](ClO_4)_2$ [15] was used in the nitrobenzene experiments and the iodide [7] in the alcohol and alcohol–water solvents.

Solvents.—Nitrobenzene was stored over phosphoric oxide for four weeks and then thrice redistilled (b. p. *ca.* 100°/1—2 mm.). The water content was estimated (Karl Fischer method) to be *ca.* 80 mg. of water/l. Further drying for three days and subsequent distillation did not reduce the water content appreciably.

Purified and " dried " ethanol [16] was estimated to contain *ca.* 180 mg. of water/l. (Karl Fischer method). No great care was taken in the drying of methanol as it was only used mixed with water.

Buffer Mixtures.—Buffers containing potassium ion were avoided because of interference

[8] Neumann, reported in ref. 7, p. 1331.
[9] Basolo, Hayes, and Neumann, *J. Amer. Chem. Soc.*, 1954, **76**, 3807.
[10] Brinzinger, Fallab, and Erlenmeyer, *Helv. Chim. Acta*, 1955, **38**, 557.
[11] Davies and Dwyer, *Trans. Faraday Soc.*, 1954, **50**, 820.
[12] Johnson and Hall, *J. Amer. Chem. Soc.*, 1948, **70**, 2344.
[13] Stranks and Wilkins, *Chem. Rev.*, in the press.
[14] Ellis, Wilkins, and Williams, *J.*, 1956, 3975.
[15] Dwyer and Gyarfas, *J. Proc. Roy. Soc. New South Wales*, 1949, **83**, 232.
[16] Adickes, Brunnert, and Lücker, *Ber.*, 1930, **63**, *B*, 2753.

by precipitation of potassium perchlorate in the separation procedure. In the 5·6—7·0 pH range, NaH_2PO_4–Na_2HPO_4 mixtures were used; for measurements at pH 9·6—9·7, sodium barbiturate–HCl or sodium borate–HCl buffers were used. Sodium hydroxide solutions were prepared from conductivity water and rinsed sodium hydroxide pellets. pH was measured with a Pye " Universal " pH meter and millivoltmeter.

Counting Procedure.—This was essentially as described in Part I.

Exchange Experiments.—Since anions which precipitate $[Ni\ phen_3]^{2+}$, *e.g.*, $PdCl_4^{2-}$ or ClO_4^-, tend to precipitate phenanthroline, it was necessary to separate the free phenanthroline from the complex, which was substantially complete after two extractions with benzene. The complex remaining in the aqueous solution was precipitated as the sparingly soluble $[Ni\ phen_3](ClO_4)_2,3H_2O$ [2, 15] by adding sodium perchlorate. The phenanthroline in the benzene extract was converted into $[Ni\ phen_3](ClO_4)_2$ so that direct comparison of the activities was possible. (This was not absolutely necessary but it was a fairly simple means of obtaining the phenanthroline in reproducible form.) In a typical run solid phenanthroline (0·1—0·2 g.) was added to the buffer or alkaline solution (60—120 c.c.) and kept overnight at 45° to dissolve. A weighed quantity of the radioactive nickel complex (0·1—0·3 g.) was added and dissolved by vigorous shaking. This rarely took longer than 1 min. In several runs an aliquot part (10—20 c.c.) was immediately taken (zero-time) and further aliquot parts removed after various times. A final portion was allowed to reach exchange equilibrium (usually 24 hr.). Each aliquot portion was quickly shaken with benzene (1 × 25 c.c. and 2 × 15 c.c.), and nickel nitrate

TABLE 1. *Exchange of* $[Ni\ phen_3]^{2+}$ *with phenanthroline under various conditions.*

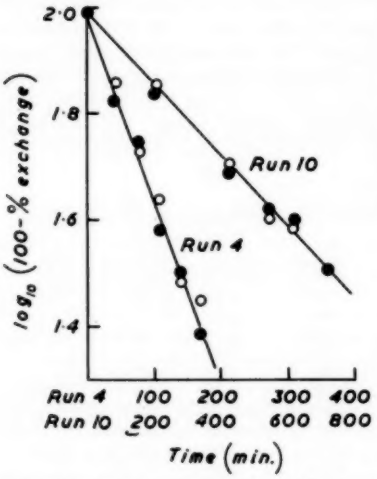
Run No.	Solvent and conditions	Temp.	[Complex] (mmole l.$^{-1}$)	[Phen] (mmole l.$^{-1}$)	$t_{\frac{1}{2}(exch)}$ (min.)	10^5R (min.$^{-1}$ mole l.$^{-1}$)	$10^4k_{(exch)}$ (min.$^{-1}$)	$10^4k_{(rac)}$ min.$^{-1}$
1	pH = 7·0	45·1°	3·05	11·10	118	2·95	96·7	93·6
2	pH = 7·0 [a]	45·1	3·15	11·31	127	2·81	89·5	
3	pH = 7·0 [a]	45·1	3·04	11·26	129	2·70	89·0	
4	pH = 7·0 [a]	45·1	5·92	11·41	86	5·60	94·6	
5	pH = 7·0 [a]	45·1	1·59	11·54	144	1·62	102·0	
6	pH = 7·0 [a]	45·1	3·28	21·48	151	3·09	94·5	
7	pH = 7·0 [a]	45·1	2·13	5·98	100	2·14	100·5	
8 [b]	pH = 7·0 [a]	45·1	3·27	6·02	90	2·88	88·0	
9	pH = 7·0 [a]	45·0	3·60	13·16	127	3·24	90·0	91·2
10	pH = 7·0 [a]	35·0	3·19	13·10	435	0·88	27·6	
11	pH = 7·0 [a]	35·0	3·12	11·43	430	0·83	26·6	
12	pH = 7·0 [a]	55·0	3·34	11·50	35	10·70	302·0	
13	pH = 9·7 [c]	45·0	2·96	13·37	149	2·51	78·9	77·0
14	pH = 9·6 [d]	44·9	3·16	13·76	130	3·00	95·0	
15	pH = 5·7 [a]	45·0	3·23	12·88	129	2·98	92·3	
16	0·01M-NaOH	44·9	3·18	11·60	121	2·83	94·0	92·4
17	pH = 13·4	45·0	3·23	11·55	55	6·59	204·0	
18	pH = 13·3	45·0	3·21	11·59	58	6·83	212·7	112·0
19	0·087M-NaOH	45·0	2·85	9·64	99	3·18	111·2	
20	0·097M-NaOH	45·0	2·82	9·27	96	3·19	113·0	110·8
21	0·129M-NaOH	45·0	2·82	9·74	90	3·49	123·0	
22	Nitrobenzene	45·3	6·86	1·52	940	0·104	1·52	1·57
23	Nitrobenzene	45·3	5·37	1·95	1760	0·069	1·28	1·34
24	Ethanol	45·3	5·92	2·14	82	1·62	27·4	29·5
25	Ethanol–water [e]	45·3	5·82	2·07	25·5	5·04	86·5	86·0
26	Methanol–water [e]	45·3	5·80	1·97	20·5	5·97	102·5	92·5

[a] Phosphate buffer, $\mu = 0·36$. [b] Diffuse light. [c] Barbiturate buffer, $\mu = 0·36$. [d] Borate buffer, $\mu = 0·36$. [e] Mole-fraction: Alcohol, 0·3, water 0·7.

solution (8·5 mg., 5 c.c.) added to the combined benzene extracts. The benzene was almost evaporated and the aqueous solution of the complex remaining separated from the benzene layer. Sodium perchlorate added to this aqueous solution and to the original solution after removal of the phenanthroline precipitated the complex perchlorate, which was washed twice with small amounts of water and dried in a vacuum desiccator overnight (P_2O_5). It was then washed with ethyl acetate to complete removal of sodium perchlorate, dried in an oven at about 80°, and prepared for counting as previously described.[4] In one run (No. 11, Table 1) active phenanthroline and inactive complex were used and a similar result was obtained to that by the

more usual method. In the experiments in nitrobenzene, separation was easily affected by addition of benzene which precipitated the complex perchlorate, from which traces of phenanthroline could be removed by washing with several portions of benzene. In the experiments in ethanol, ethanol–water, and methanol–water, the complex was precipitated by ether. In all cases, very small " zero-time " exchange values confirmed the effectiveness of the separation procedures.

Racemisation Experiments.—These were all performed at 45°, a complex concentration of about 10^{-3}M being used. In the work on aqueous solutions some parallel racemisation and exchange runs were performed in, as far as possible, identical conditions (see Table 1). However, because of difficulty in reproducing results, especially in nitrobenzene, the racemisation and exchange rates in alcohol and in nitrobenzene were measured in the same run, *i.e.*, with optically active complex and radioactive phenanthroline. A decimetre polarimeter tube and a Hilger polarimeter (sodium D line) were used for all measurements, and in all kinetic work the temperature was maintained constant within ±0·03°.



Results from: ○ complex activities, ● phenanthroline activities.

Calculation of Results.—Log [1 − (fraction of racemisation)] was plotted against time, and the racemisation half-life, $t_{\frac{1}{2}(\mathrm{rac})}$, read off directly from the linear plot. The racemisation rate constant $k_{\mathrm{rac}} = 0{\cdot}693/t_{\frac{1}{2}(\mathrm{rac})}$ was then calculated; in this form the value can be related directly to the dissociative rate constants obtained from the exchange results.[2,3] The exchange rate, R, is given by:

$$R = \frac{0{\cdot}693}{t_{\frac{1}{2}(\mathrm{exch})}} \cdot \frac{3[\mathrm{complex}][\mathrm{phen}]}{(3[\mathrm{complex}] + [\mathrm{phen}])}$$

where $t_{\frac{1}{2}(\mathrm{exch})}$ is read directly from the linear log [1 − (fraction of exchange)]–time plot.[17] Some experimental plots are given in the Figure. Davidson and Sullivan [18] have discussed the choice of the optimum times of exchange so that errors in the estimated exchange rates may be minimised. It is assumed, justifiably, that most of the error resides in the radio-assay of the separated exchange reactants. Where 3[complex]/[phen] lies between 2 and 0·5, as in nearly all our experiments, the best separation time to use is $1{\cdot}4 \times t_{\frac{1}{2}(\mathrm{exch})}$ or 60% exchange. In all our runs therefore at least three values were obtained between one and two half-lives and, when necessary, more weight was given to these points when constructing the graph. In most runs, the reported $t_{\frac{1}{2}(\mathrm{exch})}$ is the mean of two values, one obtained from counting the separated complex activity, and the other from examining the separated phenanthroline (as a solid complex). Usually the specific activity, at equilibrium, of the two separated reactants agreed within the experimental error of sample preparation of about 4%. In some of the later experiments however the equilibrium specific activities of both reactants were consistently 5—10% less than that calculated from the known specific activity of the originally active complex and the equivalents of phenanthroline in the complex and that added in the free state. This was due to water in the nickel complex, which caused the concentration of active complex ion to be less than that estimated from the weight added. Such difficulties did not arise if the exchange was carried out as follows: a standard solution of nickel nitrate was mixed with excess of phenanthroline (6 : 1 mole ratio) and, when formation of $[\mathrm{Ni\,phen_3}]^{2+}$ was complete, exchange was initiated by the addition of a small amount of the original complex (p.1764). Close agreement of experimental and theoretical equilibrium specific activities was then obtained. This is by far the best approach, and will be adopted, when applicable, in subsequent studies.

Species present in the Exchange Runs.—Except in run 15 (Table 1), at least 99% of the

[17] Wahl and Bonner, " Radioactivity Applied to Chemistry," Chapman and Hall, Ltd., London, 1951, pp. 7 *et seq.*

[18] Davidson and Sullivan, *J. Amer. Chem. Soc.*, 1949, **71**, 739.

phenanthroline was present as the free base ($pK = 4.96$ [19]). In run 15 the molarity of phenanthroline recorded represented the sum [phen] + [phen H^+]. In runs 2—12, which were used to determine concentration dependence and the energy of activation, the ionic strength was maintained at the arbitrary value of 0·36M, which included buffer and added sodium nitrate. In all the experiments in aqueous solution it can be shown by calculation that [Ni $phen_3$]$^{2+}$ is the predominant complex ion present, the advantageous circumstance that excess of free phenanthroline is always present being borne in mind (log $K_1 = 8.6$; log $K_2 = 8.1$; log $K_3 = 7.6$ from spectrophotometric data [20]). The similar spectra of the exchange mixture in aqueous alkaline, nitrobenzene, and alcohol as well as in neutral aqueous solutions indicated that the trisphenanthroline nickel ion was the predominant species in all the exchange runs. Cryoscopic molecular-weight determinations of [Ni $phen_3$]$(ClO_4)_2$ in nitrobenzene indicated that it was substantially ionised. This was supported by conductivity measurements in the same solvent (molecular conductivity of a 3×10^{-3}M solution = 57 mhos). Run 9 (Table 1) showed that no new nickel species of different exchangeability were formed in aqueous solution during an exchange experiment: inactive complex and inactive phenanthroline were mixed in aqueous solution and kept for about 24 hr.; exchange was then initiated by injecting a small amount of the original (active) complex. A very similar rate constant was obtained to that resulting from an exchange reaction carried out without previous "ageing."

Results and Discussion

Aqueous Solution.—The results of the exchange study are recorded in Table 1 and a summary of them and a comparison with racemisation rates given in Table 2. It having been established that phosphate buffers and ionic strength had little effect on the exchange

Table 2. *Exchange and racemisation results for* [Ni $phen_3$]$^{2+}$ *in various solvents at* 45°.

Solvent	$10^4k_{(exch)}$ (min.$^{-1}$)	$10^4k_{(rac)}$ (min.$^{-1}$) this work	$10^4k_{(rac)}$(min.$^{-1}$) extrap. from previous workers' results
Water: pH = 7 *	95 *	91	89,[5] 93 [2]
pH = 13	113	111	—
Ethanol	27	29	31 [7]
0·7 Mole-fraction of ethanol	87	86	87 [7]
0·7 Mole-fraction of methanol	102	93	—
Nitrobenzene	1·24	1·34	11·3 [7]
	1·52	1·57	11·3 [7]

* At 35·0°, $10^4k_{(exch)} = 27$ and $10^4k_{(rac)} = 31$ (ref. 2).

rate (runs 1 and 2), the conditions chosen to study the variations of R with the concentrations of the exchanging species were pH 7·0 and ionic strength 0·36 M (runs 2—9) at 45·1°. As expected the results indicated a first-order dependence of R on the concentration of [Ni $phen_3$]$^{2+}$ and a zero-order dependence on the concentration of phenanthroline. This is also shown by the reasonable constancy of the rate-constant, k, in the equation $R = k$[Ni $phen_3^{2+}$]. From additional exchange rates at 35° and 55° the energy of activation and the PZ factor were estimated as 25·2 kcal./mole and 1.6×10^{15} min.$^{-1}$ respectively. Comparison with the corresponding quantities for the racemisation (24·9[5] and 25·0[2] kcal./mole and 1.2×10^{15} [5]), in addition to the results in Table 2, prove that the same path accommodates both processes, *viz.*, removal of one phenanthroline molecule:

$$[Ni\ phen_3]^{2+} \rightleftharpoons [Ni\ phen_2]^{2+} + phen \qquad (A)$$

or

$$[Ni\ phen_3]^{2+} + 2H_2O \rightleftharpoons [Ni\ phen_2(H_2O)_2]^{2+} + phen \qquad (B)$$

It is then necessary only that the intermediate (A) or (B) racemises rapidly compared with the rate of re-formation [2, 11] of [Ni $phen_3$]$^{2+}$.

[19] Kolthoff, Lee, and Leussing, *J. Amer. Chem. Soc.*, 1948, **70**, 2348.
[20] Margerum, Bystroff, and Banks, *ibid.*, 1956, **78**, 4211.

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No variation of the exchange-rate constant with hydrogen-ion concentration was observed from pH 5·7 to 11·7 (runs 14—16) although a slight but definite enhancement of rate was observed in 0·1M-sodium hydroxide (runs 19—21). Once again comparison with the rate of racemisation under the latter conditions indicated that the two rate constants were similar (Table 2). Thus the results of Basolo, Hayes, and Neumann [2] are confirmed and amplified over a wide pH range.

Two points in connection with the aqueous exchange study are worth mention. Both the exchange and racemisation rate were unexpectedly lowered at pH 9·7 when a sodium barbiturate–hydrochloric acid buffer mixture was used (run 13). Davies and Dwyer [21] found that the racemisation of $[Ni\ phen_3]I_2$ was considerably retarded by the presence of large anions and cations, whether optically active or not. Thus, for example, k_{rac} at 25° in water ($= 6{\cdot}70 \times 10^{-4}$ min.$^{-1}$) was reduced to $3{\cdot}26 \times 10^{-4}$ min.$^{-1}$ in the presence of 2% of ammonium naphthalene-1-sulphonate, an effect rather more pronounced than our own, which was observed with an M/15 or approximately 1% buffer solution. The suggestion [21] that considerable inhibition of ligand dissociation is caused by the presence of clusters of large ions appears reasonable in view of the close agreement of the two lowered rates.

We obtained, using one sodium hydroxide solution sample (runs 16 and 17), a marked enhancement of the exchange rate without a parallel change in the racemisation rate, using the same hydroxide solution but different reaction vessels. Subsequent work with use of fresh alkali solutions (runs 19—21 are only representative examples) never revealed this effect again; we ascribe it to catalytic impurities. Adamson and Basolo [22] noted in the hydrolysis of $[Co(NH_3)_5Cl]^{2+}$ and $[Co(NH_3)_5Br]^{2+}$ that unless very pure sodium hydroxide was used irreproducible and generally high rates resulted. Exchange of [^{14}C]dipyridyl with $[Ni\ dipy_3]^{2+}$ in water gave a dissociative rate constant $k = 14{\cdot}6 \times 10^{-2}$ min.$^{-1}$ at 25° and an energy of activation = 22·8 kcal./mole.[23] When these values are compared with racemisation values, $14{\cdot}0 \times 10^{-2}$ min.$^{-1}$,[24] and 21·8,[2] 21·9,[6] and 24·0 [23] kcal./mole, respectively, it can be seen that, despite the dependence of rates on pH, dissociation accounts for the racemisation of this ion also.

Non-aqueous Solution.—No attempt was made to study fully the exchange behaviour of $[Ni\ phen_3]^{2+}$ in other solvents, our purpose being to compare dissociation (as shown by exchange) and racemisation rates directly. In the racemisation runs in ethanol and alcohol–water close agreement with published racemisation rates was obtained and the dissociative exchange rate constant (runs 24—26) calculated from the assumed rate law, $R = k[Ni\ phen_3^{2+}]$, showed that in all these solutions a dissociative process accounted, once again, for the racemisation. (Dr. Neumann [25] has kindly supplied us with his results in 70 mole % of methanol and although preliminary work indicated a real difference between the racemisation and acid dissociation rates there were inherent difficulties in obtaining accurate rate constants and the work was abandoned.)

Some difficulty was encountered with nitrobenzene. Our racemisation rates were some ten-fold slower than those of Davies and Dwyer.[7] This rate was enhanced by added phenanthroline or water and then became somewhat irreproducible. We therefore carried out our exchange and racemisation experiments *under the same experimental conditions* and despite some variation in the rates (cf. runs 22 and 23) the rate constants were identical within experimental error. Even in nitrobenzene then, despite the unsatisfactory quantitative features of the experiments the dissociative mechanism persists. The dissociation process in aqueous solution undoubtedly involves participation of water molecules. One of the difficulties in discussing this process in " anhydrous " solvents is connected with the presence of water which Karl Fischer determination indicated as about 0·01M (in alcohol) and 0·005M (in nitrobenzene). This means that water is present in

[21] Davies and Dwyer, *Trans. Faraday Soc.*, 1954, **50**, 24.
[22] Adamson and Basolo, *Acta Chem. Scand.*, 1955, **9**, 1261.
[23] Wilkins and Ellis, unpublished work.
[24] Davies and Dwyer, *Trans. Faraday Soc.*, 1953, **49**, 180.
[25] Neumann, personal communication.

concentrations comparable with the exchange reactants so that a similar dissociation process to that which takes place in aqueous solution cannot be ruled out. Only very dry solvents and special precautions to exclude moisture during the measurements could resolve this ambiguity.

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THE UNIVERSITY, SHEFFIELD. [*Received, September 25th*, 1956.]

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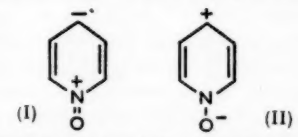
334. *The Electric Dipole Moments of a Series of 4-Substituted Pyridines and Pyridine 1-Oxides.*

By A. R. KATRITZKY, E. W. RANDALL, and L. E. SUTTON.

The dipole moments of some compounds indicated in the title have been measured. Together with values for substituted alkanes and benzenes they afford evidence that the pyridine 1-oxide ring can create either a surfeit or deficit of electrons at the 4-position.

LINTON [1] showed that the difference (2·02 D) between the dipole moments of pyridine 1-oxide (4·24 D) and pyridine (2·22 D) was much less than the difference (4·37 D) between the dipole moments of trimethylamine oxide (5·02 D) and trimethylamine (0·65 D), and pointed out that structures such as (I) must therefore be important contributors to the resonance hybrid of this molecule. Ochiai [2] and independently den Hertog and Overholt [3]



(I) (II)

demonstrated that this facilitated electrophilic substitution in the γ-position, and their observations have led to the opening of a new field of heterocyclic chemistry (for general review see ref. 4). Ochiai [2] later gave chemical evidence that structures such as (II) also contributed to the resonance hybrids of pyridine 1-oxides, but this has not yet been supported by dipole moment evidence. It was felt that comparison of the dipole moments of a series of substituted benzenes, pyridines, and pyridine 1-oxides might be illuminating.

EXPERIMENTAL

Preparation and Purification of Materials.—Benzene of analytical-grade was purified as described by Hill and Sutton.[5]

The preparation has already been described [6] of 4-chloro-, 4-acetyl-, and 4-ethoxycarbonylpyridine 1-oxide; the compounds were recrystallised two or three times more, immediately before measurement of their moments. The following preparation was more advantageous than that described [6] for 4-dimethylaminopyridine 1-oxide. 4-Chloropyridine 1-oxide (5 g.) and aqueous dimethylamine (30% w/v; 30 c.c.) were heated for 18 hr. (sealed tube). Potassium carbonate (5 g.) was added, the whole evaporated at 100°/14 mm., and the residue extracted with ethyl acetate. The extracts deposited 4-dimethylaminopyridine 1-oxide (93%), usually as a new *polymorph*, which after recrystallisation from ethanol–ethyl acetate

[1] Linton, *J. Amer. Chem. Soc.*, 1940, **62**, 1945.
[2] Summarizing paper: Ochiai, *J. Org. Chem.*, 1953, **18**, 534.
[3] den Hertog and Overholt, *Rec. Trav. chim.*, 1950, **69**, 468.
[4] Katritzky, *Quart. Rev.*, 1956, **10**, 395.
[5] Hill and Sutton, *J.*, 1949, 746.
[6] Katritzky, *J.*, 1956, 2404.

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TABLE 1.

10^6w	ε	v	$10^5\Delta n_D$
4-Methoxypyridine 1-oxide			
547	2·2855	1·1444	6
1379	2·3033	1·1440	15
3246	2·3470	1·1432	36
6423	2·4184	1·1420	68
9494	2·4880	1·1407	101

$\varepsilon = 2{\cdot}2728 + 22{\cdot}68w$; $v = 1{\cdot}1446 - 0{\cdot}408w$; $\Delta n_D = 0{\cdot}00001 + 0{\cdot}106w$; $_EP = 34{\cdot}60$ c.c.; $_TP = 537{\cdot}45$ c.c.; $\mu = 5{\cdot}08 \pm 0{\cdot}01$ D.

4-Methylpyridine 1-oxide			
1358	2·3045	1·1442	14
3881	2·3609	1·1435	—
6115	2·4106	1·1427	60
7535	2·4443	1·1422	77

$\varepsilon = 2{\cdot}2731 + 22{\cdot}64$w; $v = 1{\cdot}1447 - 0{\cdot}321w$; $\Delta n_D = 0{\cdot}100w$; $_EP = 32{\cdot}61$ c.c.; $_TP = 492{\cdot}27$ c.c.; $\mu = 4{\cdot}74 \pm 0{\cdot}01$ D.

4-Dimethylaminopyridine 1-oxide *			
588	2·2939	1·1444	—
1147	2·3135	1·1442	—
1387	2·3236	1·1441	—

$\varepsilon = 2{\cdot}2726 + 36{\cdot}35$w; $v = 1{\cdot}1447 - 0{\cdot}421w$; $_EP = 43{\cdot}6$ c.c.; $_TP = 976{\cdot}0$ c.c.; $\mu = 6{\cdot}76 \pm 0{\cdot}04$ D.

4-Acetylpyridine 1-oxide			
2444	2·2934	1·1436	31
3896	2·3054	1·1432	48
6886	2·3317	1·1418	84
7933	2·3389	1·1416	99

$\varepsilon = 2{\cdot}2728 + 8{\cdot}413w$; $v = 1{\cdot}1446 - 0{\cdot}392w$; $\Delta n_D = 0{\cdot}00001 + 0{\cdot}122w$; $_EP = 39{\cdot}83$ c.c.; $_TP = 248{\cdot}89$ c.c.; $\mu = 3{\cdot}19 \pm 0{\cdot}02$ D.

4-Nitropyridine 1-oxide †			
635	2·2731	1·1443	9
667	2·2731	1·1442	—
992	2·2736	1·1441	13
1583	2·2737	1·1438	19
2004	2·2738	—	29
2050	2·2742	—	29
2077	2·2740	1·1436	—
2378	2·2743	—	30
5426	2·2768	1·1418	73
6238	2·2773	—	84
7837	2·2785	1·1406	103

$\varepsilon = 2{\cdot}2726 + 0{\cdot}751w$; $v = 1{\cdot}1446 - 0{\cdot}503w$; $\Delta n_D = 0{\cdot}00001 + 0{\cdot}130w$; $_EP = 36{\cdot}74$ c.c.; $_TP = 46{\cdot}59$ c.c.; $\mu = 0{\cdot}69 \pm 0{\cdot}02$ D.

4-Chloropyridine 1-oxide			
1725	2·2848	1·1439	14
3566	2·2979	1·1431	38
5782	2·3130	1·1421	57
7305	2·3235	1·1413	76

$\varepsilon = 2{\cdot}2729 + 6{\cdot}936w$; $v = 1{\cdot}1447 - 0{\cdot}462w$; $\Delta n_D = -0{\cdot}00003 + 0{\cdot}109w$; $_EP = 34{\cdot}01$ c.c.; $_TP = 196{\cdot}61$ c.c.; $\mu = 2{\cdot}82 \pm 0{\cdot}01$ D.

4-Ethoxycarbonylpyridine 1-oxide			
1255	2·2847	1·1442	11
3815	2·3093	1·1432	31
6020	2·3303	1·1426	48
8308	2·3523	1·1416	66

$\varepsilon = 2{\cdot}2727 + 9{\cdot}579w$; $v = 1{\cdot}1447 - 0{\cdot}363w$; $\Delta n_D = 0{\cdot}00001 + 0{\cdot}079w$; $_EP = 45{\cdot}83$ c.c.; $_TP = 341{\cdot}40$ c.c.; $\mu = 3{\cdot}80 \pm 0{\cdot}01$ D.

4-Dimethylaminopyridine			
1740	2·3012	1·1443	9
5339	2·3606	1·1436	38
6961	2·3874	1·1433	51
10,749	2·4530	1·1425	77

$\varepsilon = 2{\cdot}2721 + 16{\cdot}73w$; $v = 1{\cdot}1447 - 0{\cdot}209w$; $\Delta n_D = -0{\cdot}00003 + 0{\cdot}076w$; $_EP = 38{\cdot}82$ c.c.; $_TP = 419{\cdot}26$ c.c.; $\mu = 4{\cdot}31 \pm 0{\cdot}01$ D.

4-Acetylpyridine			
2110	2·2842	1·1442	6
8643	2·3188	1·1426	27
14,438	2·3496	1·1411	46
17,475	2·3657	1·1405	53

$\varepsilon = 2{\cdot}2728 + 5{\cdot}325w$; $v = 1{\cdot}1447 - 0{\cdot}242w$; $\Delta n_D = -0{\cdot}00001 + 0{\cdot}031w$; $_EP = 34{\cdot}22$ c.c.; $_TP = 154{\cdot}5$ c.c.; $\mu = 2{\cdot}41 \pm 0{\cdot}01$ D.

4-Nitropyridine			
2139	2·2778	1·1438	7
4100	2·2821	1·1420	12
7561	2·2900	1·1418	22
10,933	2·2975	1·1405	33

$\varepsilon = 2{\cdot}2728 + 2{\cdot}26w$; $v = 1{\cdot}1446 - 0{\cdot}381w$; $\Delta n_D = 0{\cdot}030w$; $_EP = 29{\cdot}92$ c.c.; $_TP = 82{\cdot}00$ c.c.; $\mu = 1{\cdot}58 \pm 0{\cdot}01$ D.

* Only three very dilute solutions of this compound could be obtained and so the error is larger than usual. The n_D values were not measured; $_EP$ was obtained as 44·42 c.c. from the measured mole refraction of 4-dimethylaminopyridine, 38·69 c.c., and the average increment for the N–O link, 5·74 c.c. This compares favourably with the 42·6 c.c. obtained from the values for dimethylaminobenzene, benzene, and pyridine 1-oxide, *viz.*, 40·8 c.c.,[a] 26·2 c.c.,[b] and 28 c.c. respectively.

† The error quoted is the precision error. The actual error is here liable to be much greater because of the effect of the neglect of $_AP$ upon a small moment. The $_AP$ term may be large since the molecule is comparable to *p*-dinitrobenzene and *p*-dicyanobenzene in having two large opposed group moments. *p*-Dinitrobenzene has an apparent moment of 0·63 D if the $_AP$ term of 8·2 c.c.[c] is taken as $_0P$. The figures for *p*-dicyanobenzene are 0·76 D and 11·9 c.c.,[c] respectively. The actual moment of 4-nitropyridine 1-oxide therefore appears to be indistinguishable from 0.

[a] Landolt and Börnstein, "Tabellen," Springer Verlag, Berlin, 1923, Vol. 1/2, p. 979. [b] *Op. cit.*, p. 977. [c] Coop and Sutton, *J.*, 1938, 1269.

had m. p. 223—225°. Sometimes partial melting occurred at 97°, with resolidification and then m. p. *ca.* 223° (Found : C, 60·6; H, 7·3. $C_7H_{10}ON_2$ requires C, 60·8; H, 7·1%).

The preparation of 4-acetylpyridine has also already been described; [7] refractionated, it had b. p. 91°/10 mm.

4-Methoxypyridine 1-oxide [8] was recrystallised four times from ethyl acetate and had m. p. 82—82·5° (lit.,[8] m. p. 81·5—82·5°).

4-Nitropyridine [8] was recrystallised three times from light petroleum (40—60°) and had m. p. 49·5—50·5° (lit.,[8] m. p. 50°).

4-Methylpyridine 1-oxide [8] was recrystallised three times from benzene and had m. p. 184—185° (lit.,[8,9] m. p. 185—186° and 181°).

The following method was convenient for the preparation of 4-nitropyridine 1-oxide in large quantities : 30% aqueous hydrogen peroxide (100 c.c.) was added to pyridine (100 c.c.) in acetic acid (600 c.c.). The whole was heated for 24 hr. at 65—70° ; more hydrogen peroxide (100 c.c.) was added, and the heating was repeated. The mixture was evaporated at 100°/14 mm. and the residue slowly added with cooling to a mixture of nitric acid (275 c.c. ; *d* 1·5) and sulphuric acid (350 c.c.). The whole was heated for 12 hr. on the water-bath (nitrous fumes were evolved), cooled, and poured on ice (*ca.* 700 g.). Powdered anhydrous sodium carbonate (*ca.* 1200 g.) was added as rapidly as possible until effervescence ceased, and the whole was rapidly filtered. The solid was dried on the water-bath and extracted by refluxing chloroform (3 × 2 l.); evaporation of the extracts gave 4-nitropyridine 1-oxide (142—145 g., 82—85%), m. p. 153—158°. Two recrystallisations from acetone raised the m. p. to 159·5—160·5°, unchanged by further recrystallisation.

4-Dimethylaminopyridine was prepared by heating 4-dimethylaminopyridine 1-oxide (2·92 g.), acetic acid (8 c.c.), and iron filings (1·5 g.) on the water-bath for 1 hr. Excess of concentrated aqueous sodium hydroxide was added, the mixture filtered, and the filtrate extracted with chloroform. Removal of solvent gave the crude base (2·13 g., 83%) which after three crystallisations from ethyl acetate had m. p. 112—113° (Found : C, 68·6; H, 8·4. Calc. for $C_7H_{10}N_2$: C, 68·8; H, 8·2%) (lit.,[10] m. p. 114°).

Physical Measurements.—Electric dipole moments were determined by measuring the dielectric constants, specific volumes, and refractive indices for Na_D light of benzene solutions at 25°, using the methods described by Everard and Sutton [11] for their small-scale technique, with the heterodyne-beat capacitance meter described by Hill and Sutton.[12] The meter was calibrated by assuming the value 2·2727 for the dielectric constant of benzene at 25°.[13] The pyknometer was calibrated with air-free distilled water. The refractive-index difference, Δn_D, between the solution and benzene was measured with a Pulfrich refractometer.

The computation of moments, and the notation used here, follow the pattern set by Everard, Hill, and Sutton,[14] so that no allowance has been made for atom polarisation, except where specifically stated, other than that implicit in using $[R]_D$ as the distortion polarisation. Other methods of calculating the slope, α, of the ε–w graphs, *e.g.*, that of Le Fèvre and Vine,[15] give moments which agree with those below to within the errors quoted. The results are given in Table 1.

Discussion

Everard and Sutton [16] defined the mesomeric moment (μ_m) of an aromatic compound Ar–Z as the vector difference between its dipole moment and that of its aliphatic (preferably *tert.*-butyl) analogue Alk–Z. This quantity provides a measure of the interaction between the π-electron system of the aromatic ring and the group Z (with the limitations given by Everard and Sutton [17]).

[7] Katritzky, *J.*, 1955, 2587.
[8] Boeckelheide and Linn, *J. Amer. Chem. Soc.*, 1954, **76**, 1286.
[9] Ochiai, *J. Pharm. Soc. Japan*, 1944, **64**, 72.
[10] Koenigs, Friedrich, and Jurany, *Ber.*, 1925, **58**, 2571.
[11] Everard and Sutton, *J.*, 1951, 16.
[12] Hill and Sutton, *J.*, 1953, 1482.
[13] Hartshorn and Oliver, *Proc. Roy. Soc.*, 1929, *A*, **123**, 664.
[14] Everard, Hill, and Sutton, *Trans. Faraday Soc.*, 1950, **46**, 417.
[15] Le Fèvre and Vine, *J.*, 1937, 1805.
[16] Everard and Sutton, *J.*, 1951, 2818.
[17] *Idem*, *J.*, 1951, 2821.

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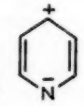
Similarly the mesomeric moment of a substituted pyridine may be defined as:

$$\mu_m Py = \mu\left(Z\text{-}C_5H_4N\right) - \left[\mu\left(C_5H_5N\right) + \mu(Alk\ Z)\right]$$

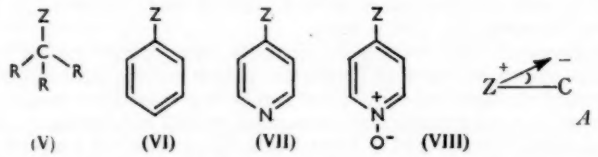
The mesomeric moment ($\mu_m O$) of a pyridine 1-oxide is defined analogously.

In pyridine the contribution of structure (III) to the resonance hybrid is far more important than that of structure (IV) (cf. the charge distribution [18]), hence it would be expected that the mesomeric moments ($\mu_m Py$) of 4(γ)-derivatives of pyridine would be

(III)  (IV)

greater than those of the corresponding benzene derivatives when Z is an electron-donating group and less when Z is an electron-accepting group. If, however, in pyridine 1-oxide the contributions of both structures (I) and (II) are sufficiently great, then it might be predicted that the mesomeric moments of 4-substituted pyridine 1-oxides ($\mu_m O$) are greater *in all cases* than those of the corresponding pyridines.

In order to calculate the mesomeric moments of a series of substituted benzenes, pyridines, and pyridine 1-oxides, the magnitudes and angles of the dipole moments of these compounds and of the corresponding substituted alkanes need to be known. Table 2 gives the magnitudes which have been measured or taken from the literature, and also the moment angles of the substituted alkanes and benzenes taken from the literature or



(V) (VI) (VII) (VIII) *A*

calculated from published data. The convention here used to define moment angles is that in the compounds (V—VIII), if the moment points along the Z–C bond, Z being the positive end of the dipole, then it has angle 0° (*i.e.*, the angle is taken as in *A*).

The directions of the dipoles of the substituted pyridines and pyridine 1-oxides are not known, and in order to calculate the mesomeric moments, the reasonable assumption has been made that the mesomeric moments in benzene, pyridine, and pyridine 1-oxide have the same direction. This not only enables the mesomeric moments to be calculated, but also gives the directions of the dipole moments of the 4-substituted pyridines and pyridine 1-oxides. The results are recorded in Table 3.

The groups NMe_2, OMe, Cl, and Me all tend to donate electrons to the benzene ring in substituted benzenes (the angles of the mesomeric moments are all about 0°), and the tendency to donate is seen to decrease in the order given. In the pyridines, in each of these cases, the mesomeric moment is greater than in the corresponding benzene, as would be expected if canonical form (III) were important, and the mesomeric moments of the pyridine 1-oxides are greater still, demonstrating the importance of canonical forms such as (II).

The groups NO_2, COMe, and CO_2Et all attract electrons from the benzene nucleus (the angles of the mesomeric moments are all about 180°), and the attraction for electrons decreases in the order given. In the corresponding pyridines, the mesomeric moment is in each case less, as is expected because of the small importance of structures of type (IV) in pyridines. In the corresponding pyridine 1-oxides, however, the magnitude of the

[18] Longuet-Higgins and Coulson, *Trans. Faraday Soc.*, 1947, **43**, 87.

TABLE 2.

Subst.	Moment magnitudes: 4-Substd. pyridine 1-oxide	4-Substd. pyridine	Substd. benzene	Substd. alkane	Moment angles: Substd. benzene	Subst. methane
H	4·24 ± 0·02 [b]	2·22 ± 0·02 [c]	0	0	—	—
Me	4·74 ± 0·01 [a]	2·61 ± 0·01 [c]	0·35 ± 0·05 [d]	0	0°	—
Cl	2·82 ± 0·01 [a]	0·78 ± 0·1 [c, k]	1·60 ± 0·01 [d]	2·01 ± 0·01 [d]	0	0°
OMe	5·08 ± 0·01 [a]	2·96 ± 0·01 [c]	1·28 ± 0·01 [21]	1·28 ± 0·01 [23]	80 [f]	124 [h]
NMe_2	6·76 ± 0·04 [a]	4·31 ± 0·01 [a]	1·61 ± 0·02 [d]	0·86 [d]	30 [d]	109 [j]
CO_2Et ...	3·80 ± 0·01 [a]	2·53 ± 0·04 [c]	1·85 [e]	1·8 [e]	110 [g]	89 [g]
COMe ...	3·19 ± 0·02 [a]	2·41 ± 0·01 [a]	2·96 ± 0·02 [d]	2·75 ± 0·05 [d]	131 [d]	120 [i]
NO_2	*ca.* 0	1·58 ± 0·01 [a]	4·01 ± 0·02 [d]	3·25 ± 0·05 [d]	180	180
CN	—[l]	1·65 ± 0·03 [c]	4·05 ± 0·01 [d]	3·60 ± 0·05 [d]	180	180

[a] Present investigation. [b] Linton's figures [1] recalculated. [c] Curran and Leis's figures [19] recalculated. [d] Taken from critical survey by Everard and Sutton.[20] [e] Selected as best available figures from data in Wesson's tables.[22] [f] With values of 2·08 (Leonard and Sutton's [24] value recalculated), 2·24 [25] and 2·23 D [26] for the dipole moments of *p*-fluoro-, *p*-chloro-, and *p*-bromo-anisole respectively, calculation by Hampson and Sutton's [27] method gave, respectively, values of 82°, 78·5°, and 78° for the moment angle in anisole.

[g] Difficulty was experienced in deducing these values. Use of Hampson and Sutton's [27] method gives discordant values: *e.g.*, Phalnikar, Bhide, and Nargund's values [28] for the moments of ethyl benzoate and its *p*-Cl, *p*-NO_2, and *p*-Br derivatives give values of 98°, 103°, and 102° respectively for the moment angle in ethyl benzoate, but Bergmann's value [29] for methyl *p*-bromobenzoate with the value for methyl benzoate [30] gives a value of 116° (no significant difference would be expected between the moment angles in ethyl and methyl benzoate). There appears to be no reliable way of deducing the direction of the moment in an aliphatic ester. In these circumstances the mesomeric moment of ethyl benzoate was assumed to be 0·50 D, at an angle of 180°, the justification being that the CO_2Et group is somewhat less electron-attracting than COMe [31] (with a μ_m in acetophenone of 0·56 D) and will have an angle near to 180°. By using these figures, it can be calculated that the moment angles in ethyl acetate and ethyl benzoate are respectively 89° and 105°. The former seems lower than would be expected, but the values are very susceptible to small differences in the assumptions made. Although the values of the mesomeric moments of 4-ethoxycarbonylpyridine and 4-ethoxycarbonylpyridine 1-oxide are also sensitive to the assumptions, it is at least clear that, provided μ_m for ethyl benzoate lies between 0·2 and 0·8 D, μ_mO in the *N*-oxide is appreciably larger than μ_mPy in the pyridine (thus if $\mu_m = 0{\cdot}2$ D, then μ_mPy = 0·03 D and μ_mO = 0·50 D, and if $\mu_m = 0{\cdot}8$ D, then μ_mPy = 0·69 D and μ_mO = 1·16 D).

[h] Calc. from ∠COC of 111° ± 3° in dimethyl ether.[32] [i] Calc. from ∠CCOof 120°.[33,34] [j] Calc. from ∠CNC of 108° ± 4° in trimethylamine.[35] [k] An allowance of 4·9 c.c. has been made for $_AP$, since this is the sum of the $_AP$ terms for chlorobenzene (3·9 c.c.[36]) and pyridine (1·5 c.c.[37]) less the $_AP$ term for benzene (0·55 c.c.[37]). [l] Because of the very small solubility of this compound in benzene and the expectation of a small moment, the determination was not attempted.

moment (μ_mO) is again greater than that of the corresponding pyridine (μ_mPy), as one would expect if structures of type (I) were important (see Figure).

An alternative way of using the dipole moment data is to consider the vector difference μ_{NO} between the moment of a substituted pyridine 1-oxide and that of the corresponding pyridine. This will give the increase or decrease in the total moment due to the attachment of oxygen to nitrogen. By using the magnitudes and angles of the gross moments

[19] Curran and Leis, *J. Amer. Chem. Soc.*, 1945, **67**, 79.
[20] Everard and Sutton, *J.*, 1951, 2807.
[21] *Idem*, *J.*, 1949, 2312.
[22] Wesson, "Tables of Electric Dipole Moments," The Technology Press, Massachusetts Institute of Technology, Cambridge, Mass., U.S.A., 1948.
[23] Groves and Sugden, *J.*, 1937, 1779.
[24] Leonard and Sutton, *J. Amer. Chem. Soc.*, 1948, **70**, 1564.
[25] Bergmann and Engel, *Z. phys. Chem.*, 1931, *B*, **15**, 85.
[26] Smyth and Walls, *J. Amer. Chem. Soc.*, 1932, **54**, 3230.
[27] Hampson and Sutton, *Proc. Roy. Soc.*, 1933, *A*, **140**, 561.
[28] Phalnikar, Bhide, and Nargund, *J. Univ. Bombay*, 1941, **10**, Pt. 3, 48.
[29] Bergmann, *J.*, 1936, 402.
[30] Phadke *et al.*, *J. Indian Chem. Soc.*, 1945, **22**, 235.
[31] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 77.
[32] Sutton and Brockway, *J. Amer. Chem. Soc.*, 1935, **57**, 473.
[33] Kimura and Kurita, *J. Chem. Soc. Japan*, 1951, **72**, 3.
[34] Allen, Bowen, Sutton, and Bastiansen, *Trans. Faraday Soc.*, 1952, **48**, 991.
[35] Brockway and Jenkins, *J. Amer. Chem. Soc.*, 1936, **58**, 2036.
[36] Groves and Sugden, *J.*, 1934, 1094.
[37] Cartwright and Errera, *Proc. Roy. Soc.*, 1936, *A*, **154**, 138.

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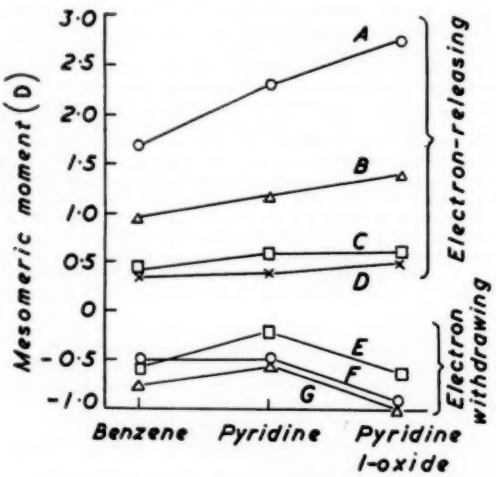
TABLE 3.

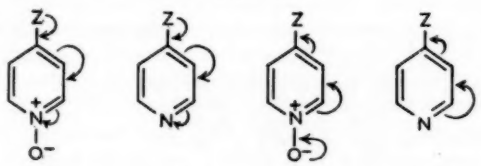
Subst.	Angle of mesomeric moment in substd. benzene	Mesomeric moment magnitudes: Substd. benzene	4-Substd. pyridine	4-Substd. pyridine 1-oxide	Gross moment angles: 4-Substd. pyridine	4-Substd. pyridine 1-oxide	Vectorial diff. between pyridine 1-oxide and pyridine moments
NMe_2 ...	0°	1·66	2·27	2·74	11°	7°	2·51
OMe ...	12	0·96	1·16	1·39	27	16	2·25
Cl	0	0·41	0·57	0·59	0	0	2·06
Me	0	0·35	0·39	0·50	0	0	2·13
H	—	—	—	—	0	0	2·02
CO_2Et ...	180	0·50	0·47	0·93	45	28	1·55
COMe ...	166	0·56	0·21	0·62	75	45	1·63
NO_2	180	0·76	0·55	0·99	0	—	1·58
CN	180	0·45	0·27	—	0	—	—

of the pyridines and pyridine 1-oxides given in Tables 2 and 3, the values of μ_{NO} given in the last column of Table 3 have been found. These moments are all at an angle of $0° \pm 1°$ (except for 3° in the case of the acetyl compounds) as would be expected. The magnitude



A, NMe_2; *B*, OMe; *C*, Cl; *D*, Me; *E*, COMe; *F*, CO_2Et; *G*, NO_2.

of 2·22 D for the difference between the moment of pyridine 1-oxide and pyridine is increased by electron-donating groups and decreased by electron-withdrawing groups. This shows that the electronic shifts indicated by the curved arrows are greater in structure (IX) than in (X) (Z being an electron-donating group) and greater in (XI) than in (XII) (Z being here an electron-accepting group).



(IX) (X) (XI) (XII)

Because electronic shifts of both type (IX—X) and type (XI—XII) are present simultaneously, and because it is impossible to calculate either separately, it should be considered whether the data might be explained by an alteration in either one or the other of these types of shift only. The two possibilities are: (i) A primary assumption that the difference in shifts (IX) and (X) is constant as Z changes. This would mean

that when Z is an electron-attracting group, shift (XI) must be more sensitive to Z than shift (XII), which is reasonable. When, however, Z is an electron-donating group, the moment due to shift (XI) less shift (XII) would have to be smaller in the Z-substituted than in the unsubstituted compounds. This could arise only if the inductive effect of Z favoured (XII) over (XI); but in fact NMe_2, OMe, and Cl all would be expected to favour (XI) at least as much as (XII). (ii) The alternative primary assumption [that the importance of shifts (XI) and (XII) is constant] is very unlikely. Whereas (XII) is known to be small, because the mesomeric moments of the pyridines with electron-attracting substituents are smaller than those in the corresponding benzenes (Table 3), (XI) must be very large, as shown by Linton's work referred to in the first paragraph of this paper, and therefore more sensitive to Z. Therefore, neither single-shift explanation is satisfactory.

It is considered that the results just discussed show that the pyridine 1-oxide ring can create either a surfeit or a deficit of electrons in the 4-position; this is in accord with the chemical evidence which shows that under suitable conditions both electrophilic and nucleophilic reagents will attack the 4-position in pyridine 1-oxides.

This work was carried out during the tenure by one of us (A. R. K.) of an I.C.I. Fellowship.

THE DYSON PERRINS LABORATORY AND THE PHYSICAL CHEMISTRY LABORATORY,
OXFORD. [*Received, October 15th*, 1956.]

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335. *Metal-ion Catalysis and Specific Kinetic Salt Effects in the Alkaline Hydrolysis of Half-esters of Dicarboxylic Acids.*

By J. I. HOPPÉ and J. E. PRUE.

The rates of alkaline hydrolysis of potassium ethyl oxalate, malonate, adipate, and sebacate have been studied in the presence of potassium, sodium, lithium, thallous, calcium, barium, and hexamminocobaltic cations. The multivalent ions and the thallous ion catalyse the hydrolysis of the oxalate and malonate esters, and the alkali-metal ions have a marked negative specific salt effect on the rates of reaction of the adipate and sebacate. The catalytic effects are ascribed to the chelation of metal ions with the transition state, and the negative specific salt effects to the separation of the charge of the ester ion from the reaction centre. The catalytic effects are analysed quantitatively.

THERE has recently been considerable interest in the catalysis of reactions by metal ions [1] and in the large specific kinetic salt effects [2] which sometimes occur. It seemed that the rates of alkaline hydrolysis of half-esters of the type $EtO_2C{\cdot}[CH_2]_n{\cdot}CO_2^-$ in the presence of various cations might throw further light on both these phenomena, and we now report a study of them.

EXPERIMENTAL

Materials.—Potassium ethyl oxalate and potassium ethyl malonate, prepared from the diethyl esters by Nielsen's method,[3] were recrystallised from absolute ethanol, dried in a vacuum desiccator, and estimated to be 99% pure by complete hydrolysis with excess of potassium hydroxide and back-titration with hydrochloric acid. Further recrystallisation did not improve their purity. Potassium ethyl adipate and potassium ethyl sebacate, prepared from the diethyl esters by Walker's method,[4] were dried in an oven, stored in a vacuum desiccator, and found to be 99·6 and 99·8% pure respectively by potentiometric titration against hydrochloric acid.

Carbonate-free sodium hydroxide solution was prepared by dilution of a concentrated

[1] Prue, *J.*, 1952, 2331.
[2] Kilpatrick, *Ann. Rev. Phys. Chem.*, 1951, **2**, 269.
[3] Nielsen, *J. Amer. Chem. Soc.*, 1936, **58**, 206.
[4] Walker, *Proc. Roy. Soc.*, 1906, *A*, **78**, 157.

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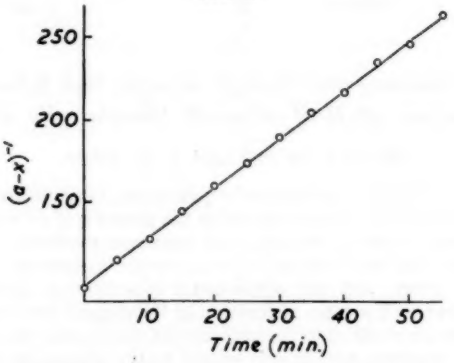
stock solution, and carbonate-free potassium hydroxide by reaction of potassium iodide with excess of silver oxide. The solutions were stored in Polythene bottles and standardised against "AnalaR" potassium hydrogen phthalate. The potassium, sodium, barium, and calcium chloride used were "AnalaR" samples. Lithium chloride and thallous nitrate were B.D.H. products, the thallous nitrate containing 1% of acidic impurity which was neutralised with potassium hydroxide. Kahlbaum's hexamminocobalt trichloride was used without further purification; a B.D.H. product was purified by Bjerrum's procedure.[5] All solutions were prepared with water of conductivity 10^{-7} ohm^{-1} cm.$^{-1}$ from an ion-exchange column.

Apparatus and Procedure.—We used a sampling technique and followed the decrease in alkali concentration titrimetrically as the reaction proceeded. The usual procedure of withdrawing samples with a pipette from the reaction mixture in a thermostat has several disadvantages, such as the danger of contamination by carbon dioxide and timing errors arising from difficulties of transfer. The reaction vessel was a 100 ml. glass syringe fitted into a glass water-jacket through which water was pumped from a thermostat tank at 25° ± 0·01°. The temperature of solutions in the syringe could be maintained within ±0·01° of this temperature which was checked by a Beckmann thermometer which had been compared with a four-junction thermocouple standardised by the National Physical Laboratory. Water was circulated through the apparatus for ½ hr. before the mixture was introduced into the syringe.

FIG. 1.



The potassium hydroxide solution, after being left in the thermostat for about 20 min., was pipetted into the ester and salt solution in a flask in the thermostat, a stop-watch being started when half the hydroxide had been delivered. (The delivery time for the 50 ml. pipette used was 20 sec.) The solution, protected by an atmosphere of nitrogen, was then rapidly drawn into the syringe through a Polythene tube and the plunger adjusted so that the extended nozzle of the syringe was free from solution. Samples of approximately 10 ml. were delivered (2—3 sec.) at suitable intervals into weighed 100 ml. glass-stoppered flasks containing an excess of potassium hydrogen phthalate solution, and the flasks were then reweighed. The solutions were back-titrated against standard sodium hydroxide solution, an atmosphere of nitrogen being maintained in the titration flask throughout. Separate experiments showed that no hydrolysis of the ester occurred in the phthalate solution.

Results.—All measurements were made with exactly equivalent concentrations a (about 0·01M) of ester and hydroxide, for which the integrated second-order rate equation has the form $(a - x)^{-1} = kt + a^{-1}$, where x is the decrease in concentration after time t and k the rate constant. Values of $(a - x)^{-1}$, equal to the concentration of hydroxyl ions present, were plotted against t, and good second-order plots obtained, in many cases up to 80% reaction. A typical plot is shown in Fig. 1 which relates to the hydrolysis of potassium ethyl adipate in 0·05M-potassium chloride. The rate constants were reproducible within 1—2%, even with times of reaction as short as 5 min. The only deviation from second-order kinetics was observed with potassium ethyl oxalate in the presence of barium ions, when the plots curved because of

[5] Bjerrum, "Metal ammine formation in aqueous solution," Haase and Son, Copenhagen, 1941, p. 241.

the precipitation of barium oxalate, but as this did not occur until the reaction was about 70% complete it was possible to determine the rate constants from the earlier points. The insolubility of calcium oxalate prevented measurements being made with ethyl oxalate in the presence of calcium.

Measurements were made with a range of metal-ion concentrations up to an ionic strength I of 0·1. The rate constants obtained are collected in Table 1. The stoicheiometric ionic strength at 50% reaction is given by adding 0·025 ± 0·002 to the contribution of the salt.

TABLE 1. *Rate constants (l. mole^{-1} min.$^{-1}$) for hydrolysis of potassium ethyl esters in presence of metal salts (molar concn. ×10^4).*

			Potassium ethyl oxalate					
KCl	—	—	136	271	407	543	679	
k	40·6	40·4	44·5	47·4	49·1	51·6	54·6	
LiCl	232	464	696					
k	48·0	52·9	57·8					
$BaCl_2$	4·3	10·7	21·4	32·1	42·9			
k	49·0	55·3	67·3	78·0	91·7			
$Co(NH_3)_6Cl_3$	130	194	259	324				
k	53·8	60·5	67·8	73·0				
$TlNO_3$	27·9	55·9	112					
k	56·8	75·6	105					
$Ba(NO_3)_2$	23·9							
k	68·0							
			Potassium ethyl malonate					
KCl	—	—	157	313	470	626	783	
k	1·05	1·05	1·15	1·21	1·25	1·30	1·34	
NaCl	234	390	468	624	780			
k	1·14	1·19	1·21	1·26	1·30			
$TlNO_3$	94	188	313	501	595			
k	1·29	1·46	1·68	1·97	2·12			
$CaCl_2$	44	89	133	177	221			
k	2·10	2·83	3·67	4·44	5·00			
$BaCl_2$	42	85	127	170	212			
k	1·36	1·56	1·69	1·81	1·92			
$Co(NH_3)_6Cl_3$	26	51	77	103	128			
k	1·28	1·49	1·63	1·75	1·86			
			Potassium ethyl adipate					
KCl	—	161	192	314	519	544	719	782
k	2·64	2·80	2·74	2·85	2·98	2·97	2·96	3·04
NaCl	83	197	249	374	559	745		
k	2·72	2·68	2·88	2·80	2·90	2·87		
LiCl	151	301	452	603	753			
k	2·73	2·88	2·86	2·87	2·86			
$TlNO_3$	168	336	504					
k	2·92	3·01	3·20					
$CaCl_2$	74	99	148	198	247			
k	2·92	3·05	3·06	3·12	3·30			
$Co(NH_3)_6Cl_3$	26	51	77	102	128			
k	2·91	3·06	3·23	3·29	3·39			
$BaCl_2$	130							
k	3·02							
			Potassium ethyl sebacate					
KCl	—	—	155	310	465	620	775	
k	1·99	1·99	2·06	2·11	2·23	2·22	2·24	
$Co(NH_3)_6Cl_3$	26	26	51	77	102	128		
k	2·19	2·13	2·25	2·38	2·41	2·47		

The reaction is one between two negative ions and the effect of the long-range Debye–Hückel interactions on k was taken into account [6] by plotting log $k^{0\prime}$, defined by

$$\log k^{0\prime} = \log k - 2AI^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

against I. The value of A, the Debye–Hückel constant, was taken as 0·509 (l. mole^{-1})$^{\frac{1}{2}}$ and the value of I as the mean stoicheiometric value for each run. Fig. 2 shows the results obtained

[6] Guggenheim and Prue, "Physicochemical Calculations," North-Holland Publishing Co., Amsterdam, 1955, p. 466.

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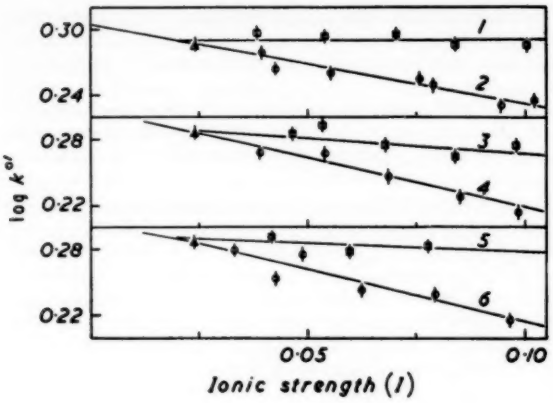
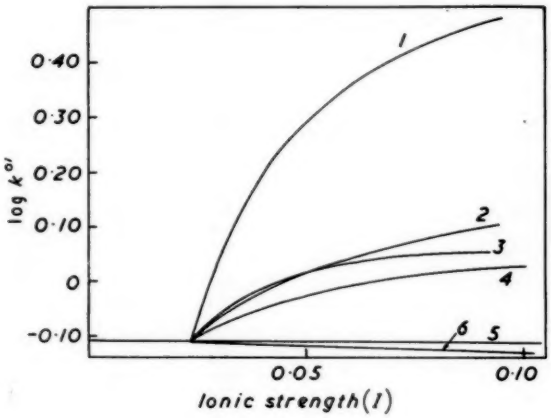


FIG. 2. Δ No added salt; 1, $Co(NH_3)_6Cl_3$; 2, KCl; 3, $CaCl_2$; 4, LiCl; 5, $TlNO_3$; 6, NaCl.

FIG. 3. Potassium ethyl malonate. 1, $CaCl_2$; 2, $TlNO_3$; 3, $BaCl_2$; 4, $Co(NH_3)_6Cl_3$; 5, KCl; 6, NaCl.



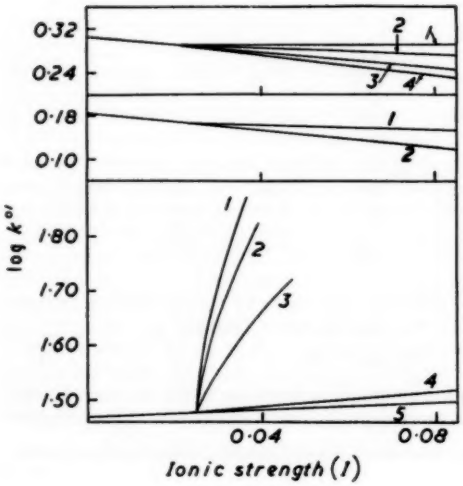


FIG. 4. Top: potassium ethyl adipate. 1, $Co(NH_3)_6Cl_3$; 2, $CaCl_2$; 3, KCl; 4, LiCl.

Middle: potassium ethyl sebacate. 1, $Co(NH_3)_6Cl_3$; 2, KCl.

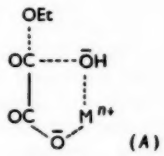
Bottom: potassium ethyl oxalate. 1, $TlNO_3$; 2, $BaCl_2$; 3, $Co(NH_3)_6Cl_3$; 4, LiCl; 5, KCl.

with potassium ethyl adipate, the vertical lines corresponding to 1½% in k. These results are typical, and all the results obtained are plotted on the same scale in Figs. 3 and 4 (the experimental points have been omitted for clarity). The effect of changing the anion of the added salt was tested by measuring the hydrolysis of ethyl malonate with barium nitrate instead of the chloride. The results were the same.

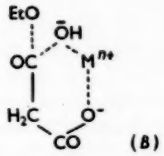
A few measurements reported in the literature [3, 7, 8] on the kinetic salt effect in the alkaline hydrolysis of half-esters in the presence of sodium or potassium ions are in general agreement with our own, but a detailed comparison is not profitable because of wide variations of temperature, ionic strength range, and accuracy. Nielsen's assertion [3] that potassium ethyl oxalate, malonate, succinate, and adipate do not show different specific effects in the presence of potassium chloride is based on an inadequate method of analysis by use of the limiting law. His results when analysed by our procedure show effects of the same magnitude as we have observed.

Discussion

The large specific effects of multivalent and thallous cations on the rates of hydrolysis of the oxalate and malonate bear no simple relation to the charge of the ion. We regard them as catalytic effects arising from the formation of chelate complexes between the metal ions and the transition state. The transition state is thereby stabilised and the energy barrier lowered. The chelate complexes may be represented as (*A*) and (*B*) and the greater effect with the oxalate is in line with the greater stability of oxalate chelate complexes (see Table 2). A similar stabilisation of the transition state by chelate formation is probably responsible for the catalysis by heavy-metal ions of the hydrolysis of amino-acid esters [9] and the large effect of calcium ions on the alkaline hydrolysis of acetylcitric and benzoylcitric acids.[10] If our interpretation is correct it follows that there are two alternative reaction paths, for one of which the transition state contains a cation as well as an ester-ion and a hydroxyl ion. We might therefore expect the second-order rate constant



(*A*)



(*B*)

k to be given by $k = k_1 + k_2[M^{n+}]$, where $[M^{n+}]$ is the concentration of the catalysing metal ion and k_1 is the rate constant of the uncatalysed reaction. In fact, plots of k against the metal-ion concentration are not linear, because of the incomplete dissociation of the hydroxides and of the metal dicarboxylates formed during the reaction. The measured rate constant is in these circumstances given by

$$k = (k_1[OH^-] + k_2[M^{n+}][OH^-])/[OH^-]_s \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$= (k_1[OH^-] + k_3[MOH^{(n-1)+}])/[OH^-]_s \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where $[OH^-]_s$ is the stoicheiometric concentration of hydroxyl ions. The constants k_2 and k_3 are related through the dissociation constant of the hydroxide. Values of k_3 have been calculated from the experimental values of k by inserting a k_1 value interpolated from the potassium chloride measurements and concentrations calculated for the mid-point of the run, account being taken of the association equilibrium by successive approximations.

[7] Westheimer, Jones, and Lad, *J. Chem. Phys.*, 1942, **10**, 478.
[8] Svirbely and Mador, *J. Amer. Chem. Soc.*, 1950, **72**, 5699.
[9] Kroll, *J. Amer. Chem. Soc.*, 1952, **74**, 2036.
[10] Smith, *Z. phys. Chem.*, 1936, **177**, 131.

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The values used for the various dissociation constants were taken from those in Table 2. Ionic activity coefficients were calculate from the Güntelberg [11] expression

$$-\log f_i = Az_i^2 I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The calculations were also carried out for ethyl adipate, although the higher-valent cations appear to be more " normal " in their salt effect than potassium. A typical set of results is shown in Table 3 for the hydrolysis of potassium ethyl malonate in the presence of

TABLE 2. *Dissociation constants (mole l.$^{-1}$).*

	Oxalate^{2-}	Malonate^{2-}	Adipate^{2-}	OH^-	Cl^-	NO_3^-
Ba^{2+}	0·0047 [a]	0·0196 [b]	0·014 [c]	0·23 [d]	—	—
Ca^{2+}	0·0010 [a]	0·0032 [b]	0·0064 [c]	0·051 [d]	—	—
$Co(NH_3)_6^{3+}$	0·0004 [e]	0·00029 [e]	0·00045 [e]	0·014 [f]	0·032 [g]	—
Tl^+	—	—	—	0·15 [h]	—	0·52 [i]

[a] Money and Davies, *Trans. Faraday Soc.*, 1932, **28**, 609. [b] Stock and Davies, *J.*, 1949, 1371. [c] Topp and Davies, *J.*, 1940, 87. [d] Bell and Prue, *J.*, 1949, 362. [e] Peacock and James, *J.*, 1951, 2233. [f] Caton and Prue, *J.*, 1956, 671. [g] Jenkins and Monk, *J.*, 1951, 68. [h] Bell and George, *Trans. Faraday Soc.*, 1953, **49**, 619. [i] Davies, *ibid.*, 1927, **23**, 351.

TABLE 3.

$10^4[BaCl_2]$	k (exp.)	$10^4[BaOH^+]$	10^4I	k_1	k_3	k (calc.)
42	1·36	60	348	1·12	30·0	1·33
85	1·56	110	471	1·17	26·0	1·55
127	1·69	155	602	1·22	23·9	1·70
170	1·81	195	730	1·26	22·4	1·83
212	1·92	225	850	1·30	21·5	1·95

barium ions. The change of k_3 with ionic strength is quantitatively in accord with expectation for a reaction between a negative ion and a positive ion and even if the small specific effect is neglected, the calculated and observed values of k are in agreement within the limits of the estimated experimental accuracy. If the calculations are carried out with use of the Davies [12] standard activity expression, which adds a linear term $0{\cdot}2Az_i^2I$ to the right-hand side of eqn. (4), the differences in the values of k_3 are less than 2%. This method of interpretation gives equally satisfactory results in the other cases. It might be thought that the changes during reaction of the various equilibria involved would cause observable deviations from second-order kinetics. Calculations show that even in the least favourable case, the experiment with the highest concentration of hexamminecobalt trichloride, the theoretical second-order rate constant would only change by 5% during the run. If experimental errors were completely absent the curvature of a second-order plot would be only just detectable, and the best straight line through the points would give a rate constant identical with that for the mid-point of the run.

Table 4 gives values of k_1^0 and k_3^0, the values of k_1 and k_3 extrapolated to $I = 0$. We

TABLE 4.

Base	Ester:	$EtOx^-$	$EtMal^-$	$EtAd^-$
OH^-		29·2	0·778	2·01
TlOH		1330	5·65	4·37
$BaOH^+$		9200	38·0	—
$CaOH^+$		—	39·8	7·94
$Co(NH_3)_6OH^{2+}$		1740	16·0	17·1

observe that k_3^0/k_1^0 varies in the order $EtOx^- > EtMal^- > EtAd^-$ which is the expected order of stability of chelate complexes. The order for the oxalate and malonate of $Ca^{2+} \sim Ba^{2+} > Co(NH_3)_6^{3+} > Tl^+$ shows the hexamminocobaltic ion to be less effective than expected by analogy with the dissociation constants in Table 2. It is possible that the ion is too large to satisfy easily the steric requirements of the transition state.

[11] Güntelberg, *Z. phys. Chem.*, 1926, **123**, 243.
[12] Davies, *J.*, 1938, 2093.

There remains to be explained the rather large but linear specific salt effects of the alkali-metal ions on the hydrolysis of ethyl adipate and sebacate. These effects are 10—20% of the total kinetic salt effect and probably arise as follows: the transition state with a carboxylate ion and a hydroxyl ion at opposite ends of a carbon chain will behave as a conventional doubly-charged ion in sufficiently dilute solution, but when the radius of the Debye–Hückel ionic atmosphere becomes comparable with the separation between the charges, each charge will tend to build up its own ion atmosphere and simulate independent ions. This means that the formation of the transition state from the free ions will be less favoured by increasing ionic strength than would otherwise be the case and a negative specific salt effect will arise. At an ionic strength of 0·1 the radius of the ionic atmosphere is about 10 Å, which is about the distance between the carboxyl groups in adipic acid. A parallel example from equilibrium studies is that the long zwitterion of methyl-orange behaves as a neutral molecule in dilute salt solution and as two separate ions in more concentrated solution.[13] We regard the very small specific effects for the ethyl adipate and sebacate reactions with multivalent cations as being due to an accidental compensation of charge separation and chelate effects.

We thank the British Rayon Research Association for a scholarship (to J. I. H.).

READING UNIVERSITY. [*Received, November 20th,* 1956.]

[13] Bjerrum, *Z. phys. Chem.*, 1923, **104**, 147.

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336. *Internuclear Cyclisation. Part XII.* The Synthesis of Some Benzophenanthridones. Abnormal Reaction of 1-Amino-N-methyl-2-naphthanilide.*

By R. A. ABRAMOVITCH, D. H. HEY, and R. A. J. LONG.

Decomposition of the diazonium chloride from 1-amino-*N*-methyl-2-naphthanilide gave the deaminated and demethylated product, 2-naphthanilide, but no 10-methyl-5 : 6-benzophenanthridone which, however, was obtained from *N*-methyl-*N*-β-naphthoyl-*o*-phenylenediamine. 10-Methyl-6 : 7-benzophenanthridone was obtained from 3-amino-*N*-methyl-2-naphthanilide. Phosphorous tri-(*N*-methylanilide) can be used to prepare *N*-methylanilides not readily available by other methods. When 2-naphthoic and benzoic acid were condensed with *N*-methyl-*o*-nitroaniline in the presence of polyphosphoric acid 4-methylamino-3-nitrophenyl β-naphthyl ketone and 4-methylamino-3-nitrobenzophenone respectively were obtained. The latter was also obtained by heating *N*-methyl-*o'*-nitrobenzanilide with polyphosphoric acid.

IN Part IX [1] it was shown that the decomposition of the diazonium salt from 2-amino-*N*-methylbenzo-1′-naphthalide gave rise to demethylation and deamination instead of to the expected cyclisation, this abnormal reaction being common to 2-amino-*N*-methylbenzanilides containing *ortho*-substituents in the anilide ring. On the other hand, 2-amino-*N*-methylbenzo-2′-naphthalide gave the corresponding *N*-methylbenzophenanthridone, cyclisation taking place at the 1′-position of the naphthalene ring. In the further application of this phenanthridone synthesis to the naphthalene series, a new abnormal reaction has now been disclosed in the attempted cyclisation of 1-amino-*N*-methyl-2-naphthanilide (V). Instead of the expected benzophenanthridone (IX), the only identifiable product was the demethylated and deaminated compound, 2-naphthanilide, which was formed together with two crystalline products, m. p. 137° and 185°, thought to be products

* Part XI, *J.*, 1954, 4263.

[1] Hey and Turpin, *J.*, 1954, 2471.

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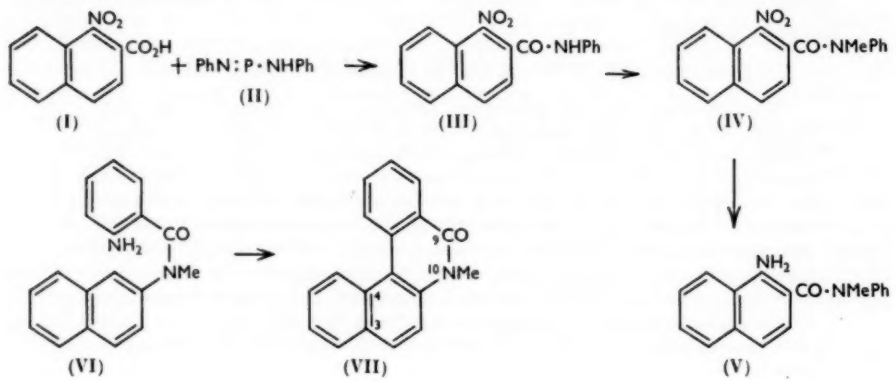
of rearrangement of the deaminated compounds. From this result it seems that a second group *ortho to the diazonium group*, as well as groups *ortho* to the anilide-nitrogen atom, can prevent normal cyclisation. This observation is being examined in greater detail.

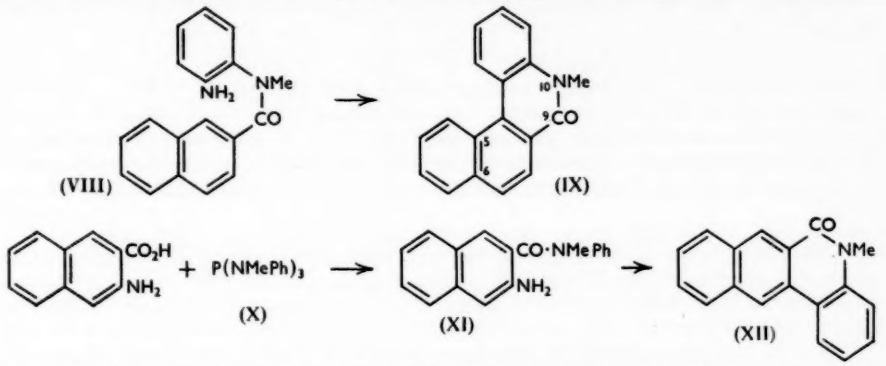
In the synthesis of 1-amino-*N*-methyl-2-naphthanilide (V) the usual route to the amide from the acid by means of the acid chloride gave inconsistent results. 1-Nitro-2-naphthoic acid (I) can be obtained in poor yield from 2-methyl-1-nitronaphthalene by conversion into the pyruvic acid followed by oxidation with permanganate.[2] The conditions of the first stage were modified to give a better yield of the pyruvic acid. In attempts to find a better route to the naphthoic acid the oxidation of 2-methyl-1-nitronaphthalene with chromic acid was examined, but this method gave a yellow product which exhibited quinonoid properties and gave a derivative with 2 : 4-dinitrophenylhydrazine. These facts, in conjunction with the analytical data, lead us to formulate this product as 7-methyl-8-nitro-1 : 4-naphthaquinone. Oxidation with permanganate also failed to give the required acid. The unexpected stability of the methyl group, unlike that in *o*-nitrotoluene, was further demonstrated by its resistance to attack by *N*-bromosuccinimide, whereas *o*-nitrotoluene, 2-methylnaphthalene, and 1-bromo-2-methylnaphthalene[3] give the bromomethyl compounds. 1-Nitro-2-naphthoyl chloride, prepared under mild conditions, reacted with aniline and *N*-methylaniline, to give the corresponding amides, but these reactions were unreliable and could not be reproduced. Another route to the amides was therefore adopted which did not involve the formation of the acid chloride. The acid (I) was condensed with the phosphazo-compound (II) from aniline[4] to give 1-nitro-2-naphthanilide (III), which was methylated and then reduced to the amine (V). Diazotisation followed by decomposition in aqueous solution gave 2-naphthanilide but no 10-methyl-5 : 6-benzophenanthridone (IX).



The alternative route to 10-methyl-5 : 6-benzophenanthridone (IX) from *N*-methyl-*N*-β-naphthoyl-*o*-phenylenediamine (VIII), in which the diazonium group is now present in the benzene ring, was next examined. The amine was obtained from 2-naphthoyl chloride by condensation with *o*-nitroaniline followed by methylation and reduction. The diazotisation of the amine was carried out in dilute hydrochloric acid at 0° in order to obviate as far as possible the formation of the benziminazole, although this could not be completely avoided. Decomposition of the cold aqueous diazonium solution with copper powder gave a benzophenanthridone, the structure of which, however, was ambiguous because of the possibility of cyclisation at the 1- or the 3-position of the naphthalene ring. Hey and

[2] Mayer and Oppenheimer, *Ber.*, 1916, **49**, 2137.
[3] Bergmann and Szmuszkovicz, *J. Amer. Chem. Soc.*, 1951, **73**, 5153; Chapman and Williams, *J.*, 1952, 5044.
[4] Grimmel, Guenther, and Morgan, *J. Amer. Chem. Soc.*, 1946, **68**, 539.

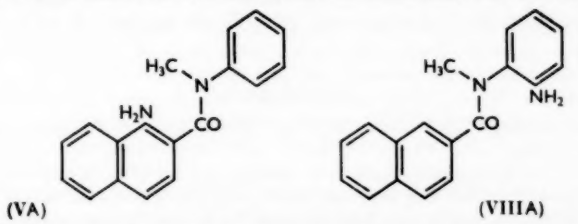
Turpin [1] showed that 2-amino-*N*-methylbenzo-2′-naphthalide (VI) gave 10-methyl-3 : 4-benzophenanthridone (VII), but on the other hand, although Weitzenböck and Lieb,[5] and also Mayer and Oppenheimer,[6] claimed to have obtained a benzophenanthroic acid from



2-amino-α-2′-naphthylcinnamic acid, Cook [7] showed that their product was in reality a mixture of two acids in which cyclisation had taken place at the 1- and the 3-position in the naphthalene nucleus.

In order to eliminate the possibility that the cyclisation product from *N*-methyl-*N*-β-naphthoyl-*o*-phenylenediamine (VIII) was 10-methyl-6 : 7-benzophenanthridone (XII), the latter was synthesised unambiguously from 3-amino-*N*-methyl-2-naphthanilide (XI), which was conveniently obtained from 3-amino-2-naphthoic acid in one stage by an extension of the phosphazo-method [4] to secondary amines. This seems to be the first time that this method has been used for the synthesis of *NN*-disubstituted amides, and it has the advantage that it can be used in cases where the amide, such as this one, would have been difficult to obtain by other methods. The reaction of phosphorus trichloride with methylaniline in hot toluene gave a product assumed to be the tri-(*N*-methylanilide) (X).[8] With anthranilic acid this gave smoothly the known 2-amino-*N*-methylbenzanilide ;[9,11] similarly with 3-amino-2-naphthoic acid it gave the required amine (XI) in moderate yield. Cyclisation of the latter gave 10-methyl-6 : 7-benzophenanthridone (XII), which was different from the product obtained from *N*-methyl-*N*-β-naphthoyl-*o*-phenylenediamine which must therefore be the 5 : 6-benzophenanthridone (IX).

The phenomenon that, in apparently very similar reactions, demethylation and deamination take place in one case and cyclisation in the other may have steric causes. The



amines (V and VIII), from which the diazonium salts are prepared, will favour the *anti*-relation for the naphthyl and phenyl groups as shown in (VA and VIIIA). The nuclear position at which the diazonium group is eliminated is thus in close proximity to the methyl

[5] Weitzenböck and Lieb, *Monatsh.*, 1912, **33**, 549.
[6] Mayer and Oppenheimer, *Ber.*, 1918, **51**, 510.
[7] Cook, *J.*, 1931, 2524.
[8] Kosolapoff, " Organophosphorus Compounds," John Wiley & Sons, New York, 1950, p. 278.
[9] Pictet and Gonset, *Arch. Sci. phys. nat. Genève*, 1897, **3**, 37.

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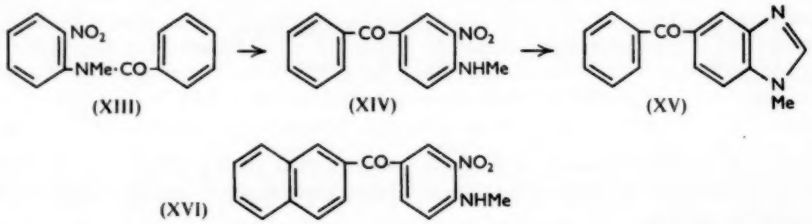
group in (VA), whereas in the isomeric amine (VIIIA) the same relation does not hold and free rotation about the N–CO bond (after elimination of the diazonium group and leading to cyclisation) is possible without impaction of the methyl group.

During this work the preparation of *N*-methyl-2′-nitro-2-naphthanilide by the direct condensation of 2-naphthoic acid and *N*-methyl-*o*-nitroaniline was investigated. Snyder and Elston [10] showed that polyphosphoric acid effected the condensation of weakly basic aromatic amines, *e.g.*, *o*-nitroaniline, with aromatic acids to give the amides. However 2-naphthoic acid and *N*-methyl-*o*-nitroaniline in polyphosphoric acid at 160° gave, in poor yield, a product isomeric with the naphthanilide obtained previously by reaction of 2-naphthoyl chloride and *o*-nitroaniline followed by methylation. A similar reaction with benzoic acid in place of 2-naphthoic acid gave, not the expected *N*-methyl-2′-nitrobenz-



(XIII) (XIV) (XV)

(XVI)

anilide, but the isomeric 4-methylamino-3-nitrobenzophenone (XIV), which was further formed when *N*-methyl-2′-nitrobenzanilide (XIII) was heated with polyphosphoric acid. The benzophenone was identified by infrared spectroscopy, by formation of a 2 : 4-dinitrophenylhydrazone, and by conversion by boiling concentrated aqueous sodium hydroxide into 4-hydroxy-3-nitrobenzophenone; further, reduction followed by boiling with formic acid gave the benziminazole (XV), proving that the methylamino- and the nitro-group are adjacent. By analogy, the product obtained from *N*-methyl-*o*-nitroaniline and 2-naphthoic acid is formulated as 4-methylamino-3-nitrophenyl 2-naphthyl ketone (XVI).

It is possible, but not necessary, that in these reactions the amide is first formed and then undergoes rearrangement to the ketone intermolecularly. This is suggested by the sublimation of benzoic acid from the reaction mixture when the pure *N*-methyl-2′-nitrobenzanilide (XIII) is used. A direct Friedel–Crafts aroylation is also possible. Similar rearrangements have been observed by Chattaway,[12] and by Dippy and his co-workers [13] when acyl, benzoyl, and dibenzoylanilides are caused to undergo rearrangement under different conditions with zinc or aluminium chlorides to the corresponding ketones. Dippy and Moss [13] postulate an intermolecular mechanism for this rearrangement. It is interesting that these authors did not obtain any identifiable products from nitroanilines under their conditions.

Experimental

Infrared measurements were carried out on a Grubb-Parsons S4 spectrometer with Nujol mulls of the compounds.

7-Methyl-8-nitro-1 : 4-naphthaquinone.—A solution of 2-methyl-1-nitronaphthalene (10 g.) in acetic acid (100 ml.) containing sulphuric acid (2 drops) was cooled in ice and treated with chromium trioxide (11 g.) during 2 hr. with stirring. The green solution was diluted with water, and the yellow solid (3·1 g.) was collected. Recrystallisation from light petroleum (b. p. 60—80°) gave *7-methyl-8-nitro-1 : 4-naphthaquinone* in yellow needles, m. p. 138° (Found: C, 60·8; H, 3·2. $C_{11}H_7O_4N$ requires C, 60·8; H, 3·2%). The product obtained on reduction gave a positve β-naphthol coupling test for a primary amine. The compound dissolved in alkali to a

[10] Snyder and Elston, *J. Amer. Chem. Soc.*, 1954, **76**, 3039.
[11] Heacock and Hey, *J.*, 1952, 1508.
[12] Chattaway, *J.*, 1904, 395.
[13] Dippy and Wood, *J.*, 1949, 2719; Dippy and Moss, *J.*, 1952, 2205.

brown solution and in mineral acid to a red solution. It formed a 2 : 4-*dinitrophenylhydrazone*, m. p. 260° (Found : N, 17·1. $C_{17}H_{11}O_7N_5$ requires N, 17·6%).

1-*Nitro*-2-*naphthylpyruvic Acid* (cf. ref. 2).—Ethyl oxalate (100 g.) was added slowly with stirring to a solution of potassium (25 g.) in absolute methanol (200 ml.) at 0°. 2-Methyl-1-nitronaphthalene (40 g.) was then added portion-wise to the stirred solution, which was allowed to reach room temperature and then stirred overnight. The suspension was heated for 1 hr. at 45° and then boiled under reflux for a further hour. To the dark-red solution cooled in ice were added water (110 ml.) and 2N-sodium hydroxide (50 ml.). The solution was filtered, the residue washed with aqueous sodium hydroxide solution, and the combined filtrates were acidified carefully with hydrochloric acid. The oil which separated solidified. The mixture was kept in the refrigerator overnight and the pyruvic acid (59 g.) collected, which, after a further purification by precipitation from alkaline solution, had m. p. 199°. Mayer (*loc. cit.*) gives m. p. 207° (decomp. 199°).

1-*Nitro*-2-*naphthanilide*.—(i) To 1-nitro-2-naphthoic acid [3] (3·3 g.) in dry acetone (50 ml.), thionyl chloride (10 g.) was added and the solution boiled under reflux for 1 hr. The acetone and excess of thionyl chloride were removed under reduced pressure and the residue was kept in a vacuum-desiccator overnight. A portion of the solid acid chloride, on recrystallisation from ether, gave needles, m. p. 120°. To the crude acid chloride in cold pyridine (50 ml.) was added aniline (1·8 ml.), and the solution was heated on a steam-bath for 3 hr. and then poured into ice-water. The solid was filtered off and recrystallisation from aqueous ethanol gave 1-*nitro*-2-*naphthanilide* (1·8 g.), m. p. 182—183° (Found : C, 69·4; H, 4·1. $C_{17}H_{12}O_3N_2$ requires C, 69·8; N, 4·1%). Various attempts to repeat this experiment failed.

(ii) The phosphazo-compound [4] (1·5 g.), prepared from aniline and phosphorus trichloride in dry toluene, and 1-nitro-2-naphthoic acid (3 g.) in dry toluene (40 ml.) were boiled under reflux for 2 hr. The hot solution was filtered and the solid, which separated on cooling, crystallised from benzene–light petroleum (b. p. 60—80°) to give the anilide (2·1 g.), m. p. 182°, undepressed on admixture with a sample obtained by method (i). Steam-distillation of the toluene mother-liquors, after treatment with aqueous sodium carbonate, gave a further quantity of the crude anilide.

N-*Methyl*-1-*nitro*-2-*naphthanilide*.—(i) *N*-Methylaniline (2 ml.) in dry acetone (50 ml.) was added to 1-nitro-2-naphthoyl chloride (from 0·5 g. of acid), and the solution boiled under reflux for 1 hr. and then poured on ice. Recrystallisation of the solid from benzene–light petroleum (b. p. 60—80°) gave N-*methyl*-1-*nitro*-2-*naphthanilide* (0·32 g.) in plates, m. p. 135—136° (Found : C, 70·8; H, 4·7. $C_{18}H_{14}O_3N_2$ requires C, 70·6; H, 4·6%). Attempts to repeat this preparation were abortive.

(ii) 1-Nitro-2-naphthanilide (1·5 g.) in acetone (10 ml.) containing 20% aqueous sodium hydroxide (10 ml.) was boiled under reflux with rapid stirring while dimethyl sulphate (2·5 ml.) was added dropwise. After boiling for 20 min. the solution was poured into ice-water; the anilide recrystallised from benzene–light petroleum (b. p. 60—80°) as plates (1·4 g.), m. p. and mixed m. p. 136°. This substance can be obtained in rigid needles, prisms (both yellow), or colourless, fluffy needles.

1-*Amino*-N-*methyl*-2-*naphthanilide*.—A solution of *N*-methyl-1-nitro-2-naphthanilide (0·7 g.) in ethanol containing 5% palladium–charcoal (0·5 g.) was hydrogenated at room temperature and pressure. The catalyst was filtered off and the solvent removed *in vacuo*. The residual colourless oil, in ether, was saturated with dry hydrogen chloride to give 1-*amino*-N-*methyl*-2-*naphthanilide hydrochloride* (0·55 g.), m. p. 170—171° after recrystallisation from ethanol–ether saturated with dry hydrogen chloride (Found : C, 68·7; H, 5·6. $C_{18}H_{16}ON_2$,HCl requires C, 69·2; H, 5·5%).

Decomposition of the Diazonium Chloride prepared from 1-*Amino*-N-*methyl*-2-*naphthanilide Hydrochloride*.—A suspension of the amine hydrochloride (1·56 g.) in ice-cold concentrated hydrochloric acid (14 ml.) and water (60 ml.) was diazotised at 0—5° with sodium nitrite (2 g.) in water (20 ml.). After being stirred for 1 hr. at 0° the mixture was diluted with water (150 ml.), treated with urea (2 g.) and then with copper powder, and stirred at room temperature overnight. A brown solid separated, and this and the mother-liquor were extracted with chloroform, the extracts being washed with alkali and dried (Na_2SO_4). The residue (1·1 g.) obtained on removal of the chloroform was chromatographed in benzene on alumina (30 × 2 cm.). Elution with benzene (600 ml.) gave a wax (0·05 g.). Benzene–ether (1 : 1) (200 ml.), followed by ether (150 ml.), gave a yellow gum (0·25 g.), which crystallised

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from ethanol to give 2-naphthanilide (0·18 g.) in plates, m. p. and mixed m. p. 170—171° (Found: C, 82·0; H, 5·5. Calc. for $C_{17}H_{13}ON$: C, 82·4; H, 5·3%). Vieth [14] gives m. p. 170°. Further elution with ether (250 ml.) gave a yellow gum (0·09 g.), which on crystallisation from benzene–light petroleum gave pale yellow prisms, m. p. 137° (Found: C, 83·2; H, 5·3%). This analysis approximates to that required for *N*-methyl-2-naphthanilide (C, 82·8; H, 5·75%), but the latter, as shown below, has m. p. 95—96°. The infrared spectrum (in Nujol mull) showed the following peaks: 3472 (broad), 1639 (s), 1608, 1585, 1560 (w), 1504 (w), 1466, 1414 (w), 1376, 1351, 1333, 1307 (m), 1101 (m), 838, 802 (w), 772 (m), and 760 cm.$^{-1}$ (s). No bands for a mono-substituted phenyl ring are present, and the analysis, spectrum, and colour seem to indicate a methylaminonaphthophenone structure. Further elution with ether (250 ml.) gave a yellow gum (0·1 g.), which did not crystallise, whereas more ether (250 ml.) gave a yellow gum (0·08 g.), which crystallised from benzene–light petroleum (b. p. 40—60°) in yellow needles, m. p. 185° (Found: C, 82·5; H, 5·7%), infrared max. (in Nujol mull) at 1689 (s), 1600 (w), 1468, 1420 (w), 1389, 1042, 1031, 1015, 905, 877, 837, 816, 803, 763 (m), 729, 686 cm.$^{-1}$ (m).

2′-Nitro-2-naphthanilide.—2-Naphthoic acid (5 g.) was boiled under reflux with an excess of thionyl chloride (10 ml.) for 1 hr. The excess of thionyl chloride was collected under reduced pressure, and the last traces removed by addition of dry benzene and vacuum-distillation. Ice-cold pyridine (10 ml.) was added to the acid chloride, and the solution treated with a solution of *o*-nitroaniline (4 g.) in pyridine (10 ml.). The orange solution was kept at room temperature overnight, heated on a boiling-water bath for 1 hr., and poured into ice-water (200 ml.). *2′-Nitro-2-naphthanilide* (7·0 g.) crystallised from ethanol in pale yellow needles, m. p. 138—139° (Found: C, 69·4; H, 3·95. $C_{17}H_{12}O_3N_2$ requires C, 69·9; H, 4·1%).

N-Methyl-2′-nitro-2-naphthanilide.—A suspension of 2′-nitro-2-naphthanilide (3·0 g.) in acetone (25 ml.) and 10% aqueous sodium hydroxide (30 ml.) was stirred and boiled under reflux. Dimethyl sulphate (4 ml.) was added dropwise and the orange solution became pale yellow. The cooled mixture was poured into ice-water, and the oil, which solidified on trituration, was washed with water. Recrystallisation from ethanol gave *N-methyl-2′-nitro-2-naphthanilide* (2·2 g.) in pale yellow plates, m. p. 124—125° (Found: C, 70·7; H, 4·55. $C_{18}H_{14}O_3N_2$ requires C, 70·6; H, 4·6%).

N-Methyl-N-2-naphthoyl-o-phenylenediamine.—The nitro-compound (3·0 g.) in warm methanol (200 ml.) was reduced with hydrogen in the presence of 5% palladium–charcoal at atmospheric temperature and pressure. The catalyst was filtered off and the solution evaporated to a small volume *in vacuo* at as low a temperature as possible. The solid which separated was washed with methanol–light petroleum, and recrystallisation from methanol gave *N-methyl-N-2-naphthoyl-o-phenylenediamine* (2·1 g.) in colourless prisms, m. p. 163—165° (Found: C, 77·9; H, 5·9. $C_{18}H_{16}ON_2$ requires C, 78·3; H, 5·8%).

Decomposition of the Diazonium Chloride prepared from N-Methyl-N-2-naphthoyl-o-phenylenediamine.—To the amine (2·1 g.) in methanol (150 ml.) at 0° was added a solution of concentrated hydrochloric acid (14 ml.) in methanol (20 ml.). Pentyl nitrite (4 ml.) was then added dropwise to the cooled stirred solution. After 4 hours' stirring at 0° copper powder (3·0 g.) was added and the mixture stirred for 18 hr., after which the evolution of nitrogen had ceased. The copper powder was filtered off and washed with hot methanol; the combined methanol solution was then evaporated to dryness under reduced pressure and the residual gum in a small volume of ethanol was adsorbed on alumina (80 g.). Elution with benzene gave a colourless gum, which crystallised from ethanol containing a few drops of benzene to give *N-methyl-5:6-benzophenanthridone* (0·20 g.) in fluffy needles, m. p. 158—159° (Found: C, 83·1; H, 5·2. $C_{18}H_{13}ON$ requires C, 83·4; H, 5·0%), $\lambda_{max.}$ 228, 231, 238, 271 mμ ($10^{-3}\varepsilon$ 45·64, 45·8, 44·91, 72·65). The m. p. was depressed to 135° on admixture with the starting amine. Elution with benzene–ether (400 ml.; 3 : 5) gave a white solid which, on crystallisation from dilute methanol, gave *1-methyl-2-2′-naphthylbenziminazole* (0·16 g.) in fine needles, m. p. 128° (Found: C, 84·4; H, 5·5. $C_{18}H_{14}N_2$ requires C, 83·8; H, 5·4%).

N-Methyl-2-naphthanilide.—The acid chloride from 2-naphthoic acid (1·0 g.) and *N*-methylaniline (0·56 g.) in dry benzene (10 ml.) were boiled under reflux for 2 hr. The solution was evaporated almost to dryness and light petroleum (b. p. 60—80°) was added until a turbidity appeared. The *anilide* separated gradually and crystallised from alcohol–light petroleum (b. p. 60—80°) in prisms (0·98 g.), m. p. 95—96° (Found: C, 82·5; H, 6·05. $C_{18}H_{15}ON$ requires C, 82·8; H, 5·75%).

[14] Vieth, *Annalen*, 1876, **180**, 305.

2-Amino-N-methylbenzanilide.—Phosphorus trichloride (9·2 g.) in dry toluene (20 ml.) was added dropwise to a stirred solution of *N*-methylaniline (42·8 g.) in dry toluene (50 ml.). The amine hydrochloride separated almost immediately. After 1 hour's stirring the mixture was heated at 100° for ½ hr., the solid dissolving. The cooled mixture was filtered and the solid washed with cold alcohol. Part of it dissolved and the insoluble residue was collected and dried. The filtrate was evaporated to dryness *in vacuo* and the solid residue washed with alcohol and combined with the first residue. The total weight of crude phosphorous tri-(*N*-methylanilide) was 16·6 g. This compound (1·18 g.), which is unstable, in dry toluene (20 ml.) was boiled under reflux for 3 hr. with anthranilic acid (1·5 g.). The hot solution was filtered from the gummy metaphosphorous acid and on concentration gave 2-amino-*N*-methylbenzanilide (0·5 g.), which crystallised from benzene in needles, m. p. 125° (Found : C, 74·4; H, 6·5. Calc. for $C_{14}H_{14}ON_2$: C, 74·6; H, 6·2%). Heacock and Hey [11] give m. p. 126—127° for this anilide prepared from *N*-methyl-2-nitrobenzanilide by reduction.

3-Amino-N-methyl-2-naphthanilide (XI).—Phosphorous tri-(*N*-methylanilide) (15 g.) in toluene (150 ml.) was boiled under reflux for 3 hr. with 3-amino-2-naphthoic acid (24 g.). The hot solution was filtered, washed with 2N-sodium hydroxide, and evaporated under diminished pressure. The residue, on crystallisation from methanol, gave the *anilide* (8·2 g.) in yellow needles, m. p. 163° (Found : C, 78·2; H, 5·5. $C_{18}H_{16}ON_2$ requires C, 78·2; H, 5·8%). It gave a positive diazo-coupling test for a primary amine and exhibited a strong absorption at 1639 cm.$^{-1}$, characteristic of the amide-carbonyl group.

Decomposition of the Diazonium Chloride prepared from 3-Amino-N-methyl-2-naphthanilide.—A suspension of the amine (1·0 g.) in concentrated hydrochloric acid (3 ml.) and water (10 ml.) was diazotised at 0° with sodium nitrite (0·5 g.) in water (10 ml.). After several hours' stirring at 0° water (200 ml.) was added and then urea (0·5 g.). The solution was treated with copper powder (1·0 g.) and stirred at room temperature for 24 hr. and then filtered. The residue and the filtrate were extracted separately with chloroform, and the combined extracts washed with alkali, dried (Na_2SO_4), and evaporated. The residual gum in benzene was chromatographed on alumina (90 g.). Elution with benzene (250 ml.) gave a gum. Elution with benzene–ether (1 : 1 v/v; 350 ml.) gave *10-methyl-6 : 7-benzophenanthridone* (0·1 g.) in fluffy needles, m. p. 180° (from methanol) (Found : C, 82·9; H, 5·5. $C_{18}H_{13}ON$ requires C, 83·4; H, 5·0%), $\lambda_{max.}$ 220, 264, 272 mμ ($10^{-3}\varepsilon$ 42·38, 62·0, 95·76). Further elution with benzene–ether (1 : 1) gave a yellow solid (0·07 g.) in fine yellow needles (from alcohol), m. p. 229° (Found : C, 77·7; H, 5·3%).

4-Methylamino-3-nitrophenyl 2-Naphthyl Ketone.—A mixture of 2-naphthoic acid (2 g.), *N*-methyl-*o*-nitroaniline (1·9 g.), and polyphosphoric acid (70 g.) was stirred while the temperature was slowly raised to 160° during 20 min. The colour changed from yellow to deep brown. The hot solution was then poured into cold water (600 ml.) and set aside overnight. The brown solid was filtered off. Crystallisation from alcohol gave the *naphthophenone* (0·2 g.) in yellow needles, m. p. 195° (Found : C, 69·8; H, 4·4. $C_{18}H_{14}O_3N_2$ requires C, 70·6; H, 4·6%), infrared max. (main peaks) at 3448, 1650 (m), 1634 (s), 1582, 1524, 1372, 1302, 1282, 758 cm.$^{-1}$.

4-Methylamino-3-nitrobenzophenone.—(i) A mixture of benzoic acid (5·1 g.), *N*-methyl-*o*-nitroaniline (6·0 g.), and polyphosphoric acid (50 g.) was stirred, heated, and worked up as in the previous preparation. Recrystallisation of the brown solid from alcohol gave the *benzophenone* (1·1 g.), m. p. 197° (Found : C, 65·4; H, 4·9. $C_{14}H_{12}O_3N_2$ requires C, 65·7; H, 4·7%), infrared max. (main peaks) at 3425, 1653 (m), 1626 (s), 1577, 1527, 1370, 1330, 1290, 1231, 766, 735, 693 cm.$^{-1}$). The 2 : 4-*dinitrophenylhydrazone* had m. p. 257° (from ethanol) (Found : C, 55·7; H, 3·7. $C_{20}H_{16}O_6N_6$ requires C, 55·0; H, 3·7%).

(ii) *N*-Methyl-2-nitrobenzanilide (5·0 g.) was stirred and heated with polyphosphoric acid (50 g.) as described above. The resulting benzophenone (0·8 g.) had m. p. 197°, undepressed on admixture with the product prepared as described in method (i) above.

4-Hydroxy-3-nitrobenzophenone.—4-Methylamino-3-nitrobenzophenone (0·1 g.) was boiled with 10N-sodium hydroxide (50 ml.) for 48 hr., a clear solution being obtained. This was cooled, acidified, and extracted with ether. Evaporation of the dried (Na_2SO_4) ether gave 4-hydroxy-3-nitrobenzophenone (0·05 g.) in needles, m. p. 90° (from methanol) (Found : C, 63·7; H, 3·9; N, 5·35. Calc. for $C_{13}H_9O_4N$: C, 64·2; H, 3·7; N, 5·8%), infrared max. (main peaks) at 3378, 3125, 1678 (s), 1626 (s), 1587, 1543 (s), 1342, 1258, 1162, 743, 703 cm.$^{-1}$. The m. p. was undepressed on admixture with a sample prepared by the method of Blakey, Jones, and Scarborough [15] (who give m. p. 94°). The 2 : 4-*dinitrophenylhydrazone* had m. p. and mixed

[15] Blakey, Jones, and Scarborough, *J.*, 1927, 2870.

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m. p. 262° [from benzene–light petroleum (b. p. 40—60°)] (Found: C, 53·9; H, 3·1. $C_{19}H_{13}O_7N_5$ requires C, 53·9; H, 3·2%). The *semicarbazone*, m. p. and mixed m. p. 178°, separated from alcohol (Found: C, 55·2; H, 3·9. $C_{14}H_{12}O_4N_4$ requires C, 55·9; H, 4·0%).

3-Amino-4-methylaminobenzophenone.—4-Methylamino-3-nitrobenzophenone (0·2 g.) was treated with the stannous chloride reagent [16] (2 ml.), heated on a water-bath for 5 min., and then left at room temperature overnight. The complex was decomposed with an excess of alkali, and the solution extracted with ether. Evaporation of the dried ethereal extract gave the *diamine*, which separated from benzene–light petroleum (b. p. 40—60°) as a yellow solid (0·12 g.), m. p. 121° (Found: C, 74·3; H, 6·0. $C_{14}H_{14}ON_2$ requires C, 74·4; H, 6·2%). It diazotised normally, but the diazonium solution did not give a positive β-naphthol coupling test, probably owing to triazole formation. The diamine (0·2 g.) was boiled under reflux with 90% formic acid (10 ml.) for 2 hr. The excess of formic acid was then removed under reduced pressure and the residue kept on a water-bath in 4N-hydrochloric acid for 1 hr. The solution was concentrated, made alkaline, and extracted with chloroform. To the dried chloroform extract light petroleum (b. p. 40—60°) was added until a slight turbidity was obtained. *5-Benzoyl-1-methylbenziminazole*, m. p. 97°, crystallised in white cubes and was recrystallised from chloroform–light petroleum (b. p. 40—60°) (Found: C, 76·2; H, 5·3. $C_{15}H_{12}ON_2$ requires C, 76·3; H, 5·1%).

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KING'S COLLEGE (UNIVERSITY OF LONDON),
STRAND, LONDON, W.C.2. [*Received, November 21st*, 1956.]

[16] Abramovitch and Hey, *J.*, 1954, 1700.

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337. *The Synthesis of Some Olefinic Acids using Tetrahydro-β-halogeno-furan and -pyran Derivatives as Intermediates.*

By M. F. ANSELL and S. S. BROWN.

The preparation of some cyclic β-halogeno-ethers is described. The alkenols obtained by their ring scission are used in syntheses of some alk-4-, -5-, and -6-enoic acids.*

FOR a survey of the intramolecular acylation of alkenoic and ω-aryl-alkenoic acids [1] we needed a general synthesis of acids of type (I; $n = 0$—2), and adopted the ring scission, with sodium, of β-halogeno-ethers (IIa or b) which gives structurally and, in some cases, stereochemically pure alkenols [2] (III; $n = 0$ or 1); these alkenols were converted into the halides and thence into the required acids.[2,3] With the exception of tetrahydrofurfuryl chloride, however, we have studied only compounds of type (IIa), as those of type (IIb) are difficult of access.[4]

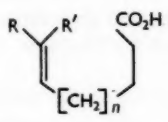
In this way we have obtained acids of type (I; $n = 0$—2) where R = R′ = H and R and/or R′ = Me. Except for three of these (I; $n = 2$, R = H, R′ = Me; $n = 1$ and 2, R = R′ = Me), they have been obtained before, but not always by methods free from stereochemical and structural ambiguity. In this respect our method is an improvement.

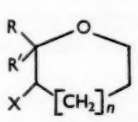
For the synthesis of pent-4-enoic acid, 3-chlorotetrahydrofuran was obtained by reduction of 2 : 3-dichlorotetrahydrofuran with lithium aluminium hydride (Crombie, Harper, Gold, and Stokes [5] reported the same reaction using "inverse" addition). Ring scission

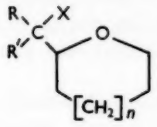
* Geneva nomenclature, $CO_2H = 1$.

[1] Ansell and Brown, *Chem. and Ind.*, 1956, 984.
[2] Crombie and Harper, *J.*, 1950, (*a*) 1707, (*b*) 1714.
[3] Cf. Linstead and Rydon, *J.*, 1934, 1995; Braude, Linstead, and Wooldridge, *J.*, 1956, 3074.
[4] Cf. *inter al.*, Eglinton, Jones, and Whiting, *J.*, 1952, 2873.
[5] Crombie, Harper, Gold, and Stokes, *J.*, 1956, 136.

with sodium gave but-3-en-1-ol,[5,6] the preparation of which by other methods is difficult.[7] For conversion of this alkenol by phosphorus tribromide and pyridine into 1-bromobut-1-ene, different authors,[7,8,9,10] using different techniques, have reported yields ranging from 30% to 78%, the lower yields probably being due, in part, to formation of dibromide (see below); but 4-chlorobut-1-ene is obtained in good yield by use of thionyl chloride in the presence of a catalytic quantity of pyridine,[9] a method probably owing its success to the


(I)


(II a)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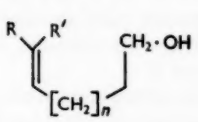
(III)

slowness of addition of hydrogen chloride to the isolated double bond (see below). Carboxylation of this halide *via* the Grignard reagent gave pent-4-enoic acid, which has been previously prepared from ethyl allylmalonate [11] and by carboxylation of the bromide obtained from *cyclo*propylmethanol.[12]

For the preparation of hex-5-enoic and hept-6-enoic acid, tetrahydrofurfuryl chloride was required. Its preparation [13] from the alcohol, pyridine, and thionyl chloride has been improved so that it involves only a catalytic amount of pyridine, with or without benzene as solvent, does not require redistilled alcohol, avoids a tedious extraction, and still gives consistently high yields of easily purified material. From the ring scission product, pent-4-en-1-ol, 5-chloropent-1-ene, and thence hex-5-enoic and hept-6-enoic acid were prepared. Both acids have been previously prepared through alkenylmalonic esters.[3,10]

Unless R = R′ (in I and III), geometrical isomerism can arise. Now stereochemically pure *trans*-alk-4-en-1-ols are obtainable from either *cis*- or *trans*-2-alkyl-3-chlorotetrahydropyrans;[2a] *trans*-hex-4-en-1-ol, from 3-chloro-2-methyltetrahydropyran,[2a] was converted into 6-chlorohex-2-ene in 80% yield and thence into *trans*-hept-5-enoic and *trans*-oct-6-enoic acid. The former acid has been previously prepared by carboxylation of the Grignard reagent obtained from 1 : 4 : 5-tribromohexane.[14] The preparation of 6-bromohex-2-ene from hex-4-en-1-ol, using phosphorus tribromide and pyridine, proceeds in only 50% yield, and gives also 15% of a dibromide, probably 1 : 4-dibromohexane. Hunsdiecker [15] reports a similar by-product in the preparation of 1-bromohex-3-ene, but suggests that it is a bromohexanol.

The route to the alk-4-enoic acids requires alk-3-en-1-ols. Preparation of these by ring scission of *cis*-2-alkyl-3-chlorotetrahydrofurans gives a mixture of the *cis*- and *trans*-isomers whilst *trans*-2-alkyl-3-chlorotetrahydrofurans yield mixtures containing mainly *trans*-isomers.[2b,5] Partial hydrogenation of alk-4-yn-1-ols, which are obtainable, although in poor yield, from 2-alkyl-3-chlorotetrahydrofurans on treatment with sodamide,[4,5] is an alternative route. We have utilised both routes. Careful fractionation of 3-chlorotetrahydro-2-methylfuran gave the *cis*- and *trans*-isomers in the ratio of 2 : 1 (in agreement with Crombie *et al.*[5]). The latter was converted, *via* *trans*-pent-3-en-1-ol (87% *trans* [5]),

[6] Cf. Yur'ev, Voronkov, Gragerov, and Kondrat'eva, *Zhur. obschei Khim.*, 1948, **18**, 1804; Yur'ev and Gragerov, *ibid.*, p. 1811; *Chem. Abs.*, 1949, **43**, 3818.
[7] Birch and McAllan, *J.*, 1951, 2556.
[8] Arbuzov and Khmel'nitskii, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1952, 766; *Chem. Abs.*, 1953, **47**, 5927; Levina and Viktorova, *Vestnik Moskov. Univ.*, **6**, No. 2, *Ser. Fiz.-Mat. i Estestven. Nauk*, 1951, **1**, 89; *Chem. Abs.*, 1952, **46**, 8605.
[9] Roberts and Mazur, *J. Amer. Chem. Soc.*, 1951, **73**, 2509.
[10] Gaubert, Linstead, and Rydon, *J.*, 1937, 1971; cf. ref. 3.
[11] Linstead and Rydon, *J.*, 1933, 580.
[12] Smith and McKenzie, *J. Org. Chem.*, 1950, **15**, 74.
[13] Brooks and Snyder, *Org. Synth.*, Coll. Vol. III, 1955, p. 698; cf. ref. 4.
[14] von Braun and Sobecki, *Ber.*, 1911, **44**, 1039.
[15] Hunsdiecker, *Ber.*, 1942, **75**, 460.

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into substantially pure *trans*-hex-4-enoic acid,* and the former, with sodamide in liquid ammonia gave pent-3-yn-1-ol in 50—55% yield—substantially higher than that reported as resulting from the *cis-trans*-mixture.[4,5] Partial hydrogenation of the pentynol gave *cis*-pent-3-en-1-ol which was converted *via* the toluene-*p*-sulphonate and iodide into *cis*-hex-4-enoic acid. This somewhat indirect route was used lest phosphorus tribromide or thionyl chloride should promote acid-catalysed *cis–trans*-isomerisation, as has been observed in the preparation of *cis*-oleyl bromide.[17] That the acid and iodide were stereochemically pure was shown by the absence of an absorption peak at 10·4 μ in their infrared spectra. The *cis*-acid so obtained was identical with that prepared by Crombie and Harper.[16]

An alternative route to *trans*-alk-4-enoic acids involves the oxidation of the readily available *trans*-alk-4-en-1-ols. Except, however, in the case of alk-2-en-1-ols, the oxidation of alkenols has rarely been used for the preparation of unsaturated aldehydes or acids. Jacobson,[18] however, has reported the rapid, low-temperature chromic acid oxidation of oct-4-en-1-ol to oct-4-enal in 35% yield. With representative alk-4-en-1-ols, in our hands, this method gave even lower yields of aldehyde, with substantial amounts of ester or lactone. *tert.*-Butyl chromate [19] proved equally unsatisfactory, whilst use of the chromium trioxide–pyridine complex [20] is limited to compounds of high molecular weight such as steroids.

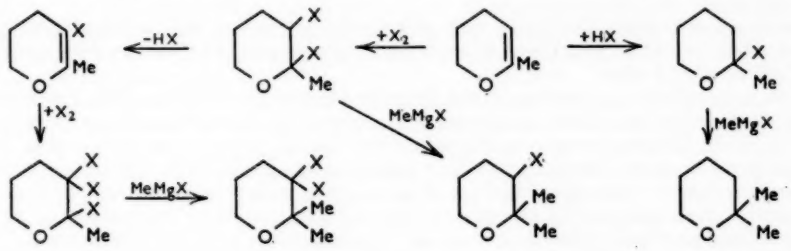
For the synthesis of acids where R = R′ = Me, 4 : 5-dihydro-2-methylfuran was prepared by the dehydrohalogenation of tetrahydrofurfuryl bromide [21] (attempts to use tetrahydrofurfuryl chloride gave unreproduceable yields of tetrahydro-2-methylenefuran [4]), and 5 : 6-dihydro-2-methylpyran from the readily accessible 5 : 6-dihydro-2-methylpyran-3-carboxylic acid.[22] The dichloro-compounds obtained by the addition of chlorine to these unsaturated compounds, although sometimes obtained pure, have been reported as unstable.[23,24] We have found it better to use the dibromides prepared at −50°; below this temperature the addition product tended to crystallise. The halides were not isolated, but were coupled with methylmagnesium bromide to yield the expected 3-halogenotetrahydro-2 : 2-dimethyl-furan or -pyran. The former product was accompanied by a higher-boiling material corresponding in analysis to a dihalogenotetrahydrodimethylfuran, whilst the latter was accompanied by lower-boiling, halogen-free material corresponding to tetrahydro-2 : 2-dimethylpyran. The formation of these by-products may be rationalised by the annexed scheme, which is given for the pyran series. Montaigne [24] records the formation of low-boiling by-product, presumably 2-ethyltetrahydro-2-methylpyran, in the reaction between ethyl Grignard reagent and 2 : 3-dichlorotetrahydro-2-methylpyran.

The ring scission of 3-chloro- or 3-bromo-tetrahydro-2-methyl-furan or -pyran proceeded equally readily (contrast the low yields obtained [25] on ring scission of 2-alkyl-3-bromotetrahydropyrans), to yield 4-methylpent-3-en-1-ol and 5-methylhex-4-en-1-ol, which from their infrared spectra were free from the *iso*propenyl isomer. [Higher yields of the alkenols might have been obtained by ring scission of the *crude* reaction mixtures (cf. refs. 5 and 26).]

* Crombie and Harper [16] showed that the acid prepared by this route (*via* 5-bromopent-2-ene) was the pure *trans*-form by comparing it with a sample prepared from (*trans*-)crotyl chloride.[16] Our acid is identical with theirs.

[16] Crombie and Harper, *J.*, 1950, 1152.
[17] Loev and Dawson, *J. Amer. Chem. Soc.*, 1956, **78**, 1180.
[18] Jacobson, *ibid.*, 1950, **72**, 1489.
[19] Oppenauer and Oberrauch, *Anales Asoc. quim. argentina*, 1949, **37**, 246.
[20] Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422; Poos, Johns, and Sarett, *ibid.*, 1955, **77**, 1026.
[21] Paul and Tchelitcheff, *Bull. Soc. chim. France*, 1950, **17**, 520.
[22] Perkin, *J.*, 1887, **51**, 702.
[23] Londergan, Hause, and Schmitz, *J. Amer. Chem. Soc.*, 1953, **74**, 4456.
[24] Montaigne, *Ann. Chim.* (*France*), 1954, **9**, 310.
[25] Brandon, Derfer, and Boord, *J. Amer. Chem. Soc.*, 1950, **72**, 2120.
[26] Riobé, *Compt. rend.*, 1955, **240**, 1648.

An attempt to convert 5-methylhex-4-en-1-ol into the chloride by using thionyl chloride and a catalytic amount of pyridine gave instead a good yield of 1 : 5-dichloro-5-methylhexane, formed by addition of the liberated hydrogen chloride to the highly reactive double bond. This alkenol, and the analogous 4-methylpent-3-en-1-ol, reacted normally with toluene-*p*-sulphonyl chloride and pyridine (no hydrogen chloride is actually set free



in this reaction [27]), to yield the toluene-*p*-sulphonates, which were converted into their iodides as for *cis*-pent-4-en-1-ol. (Attempts to prepare the alkenyl chloride or bromide by using lithium chloride or calcium bromide in boiling ethanol gave only mixtures of the required halide with the ether formed by solvolysis.) Both the iodides and the acids derived from them (5-methylhex-4-enoic, 6-methylhept-5-enoic, and 7-methyloct-6-enoic acid) showed weak infrared absorption at 11·2 μ, indicating the presence of a small amount of the *iso*propenyl isomer. Presumbably the isomerisation occurs during formation of the toluene-*p*-sulphonate. 5-Methylhex-4-enoic acid has been previously prepared from isoprene hydrobromide,[11,28a] ethyl 5-hydroxy-5-methylhexanoate,[28b] and, together with 5-methylhex-5-enoic acid,[28c] by thermal addition of acrylic acid to *iso*butene.[28d]

The present approach is immediately applicable to the synthesis of compounds derived from more elaborate Grignard reagents, *e.g.*, 2-arylethylmagnesium halides.[1]

Experimental

3-Chlorotetrahydrofuran.—2 : 3-Dichlorofuran (306 g.) (prepared by chlorination of tetrahydrofuran in methylene chloride; cf. Crombie and Harper [28b]) was added during 40 min. to a stirred suspension of lithium aluminium hydride (30 g.; 85% purity) in dry ether (1 l.) so that vigorous refluxing was maintained. The mixture was stirred and heated for a further 1 hr., and then decomposed by water (300 c.c.). The ethereal layer was washed with 10% sodium hydroxide solution and water, and dried ($CaCl_2$). The product was fractionally distilled through a column (2 × 30 cm.) packed with Dixon gauzes, to yield 3-chlorotetrahydrofuran (186 g., 81%), b. p. 129—130°, n_D^{20} 1·4545. Crombie *et al.*,[5] record b. p. 59—61°/30 mm., n_D^{20} 1·4532.

The late M. E. Selleck in this Laboratory, in agreement with Birch and McAllan,[7] found that the preparation of this alcohol from trioxymethylene and allyl chloride or bromide gives a poor yield (5—10%). (Cf. however Linstead and Rydon [3] who report a 45% yield.) The alternative preparation [7] by dehydration of butane-1 : 3-diol necessitates a careful fractional distillation.

Tetrahydrofurfuryl Chloride.—Thionyl chloride (170 g., 1·43 moles) was added slowly, with stirring, to an ice-cooled mixture of tetrahydrofurfuryl alcohol (133 g., 1·30 moles), pyridine (0·7 c.c.), and benzene (160 c.c.). When about one-half of the reagent had been added (30 min.), evolution of gas began; the remainder was then run in rapidly, without cooling, and the mixture was cautiously heated to gentle reflux, with continuous stirring. This was maintained till

[27] Edgell and Parts, *J. Amer. Chem. Soc.*, 1955, **77**, 4899.

[28] (*a*) Simon, Kaufmann, and Schinz, *Helv. Chim. Acta*, 1946, **29**, 1133; (*b*) Samokhvalov, Miropol'skaya, Vakulova, and Preobrazhenskii, *Doklady Akad. Nauk S.S.S.R.*, 1952, **84**, 1179; *Chem. Abs.*, 1953, **47**, 3277; (*c*) Eschenmoser and Frey, *Helv. Chim. Acta*, 1952, **35**, 1660; (*d*) Albisetti, Fisher, Hogsed, and Joyce, *J. Amer. Chem. Soc.*, 1956, **78**, 2637.

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acid gases were no longer freely liberated (45 min.), the mixture was then cooled and poured on excess of ice. After thorough washing (water, 5% aqueous sodium carbonate, and water) and drying ($MgSO_4$), the solvent was fractionated through a short column, and the residue distilled, to give tetrahydrofurfuryl chloride (115 g., 74%), b. p. 43—44°/13 mm., n_D^{17} 1·4566. Eglinton, Jones, and Whiting [4] record b. p. 55—56°/20 mm., n_D^{20} 1·4552.

Larger runs (up to 15 moles) were most conveniently effected without a solvent; the yields were the same.

5-Chloropent-2-ene.—This halide, b. p. 104—105°, $n_D^{18\cdot5}$ 1·4309, was prepared in 65% yield on a 4-molar scale from pent-4-en-1-ol as for tetrahydrofurfuryl chloride. Paul [29] records b. p. 105°/747 mm., n_D^{19} 1·4305.

Hex-5-enoic Acid.—A solution of the Grignard reagent prepared from 5-chloropent-2-ene (42 g., 0·40 mole) and magnesium (10 g., 0·42 g.-atom) in ether (200 c.c.) was poured on a large excess of stirred, finely powdered solid carbon dioxide. After most of the carbon dioxide had evaporated, water (300 c.c.) and light petroleum (b. p. 40—60°; 200 c.c.) were added, followed by sufficient 10N-hydrochloric acid (24 c.c., 0·24 mole) to give two clear phases. The organic layer was separated and the aqueous phase extracted with light petroleum (3 × 100 c.c.). The combined petroleum solutions were extracted with a saturated solution of sodium hydrogen carbonate (42 g., 0·5 mole), and the alkaline solution so obtained back-extracted with light petroleum and then acidified at 0° by stirring it with an equal volume of light petroleum and cautiously adding 5N-hydrochloric acid (100 c.c.). After extraction, etc., as before, distillation gave hex-5-enoic acid (34 g., 74%), b. p. 95—96°/7 mm., n_D^{20} 1·4338. Linstead and Rydon [3] record b. p. 107°/17 mm., n_D^{20} 1·4343.

cis- *and* trans-*3-Chlorotetrahydro-2-methylfuran.*—The crude reaction product [2b] from 2 : 3-dichlorotetrahydrofuran (784 g., 5·56 moles) and methylmagnesium bromide (from 168 g. of magnesium) was fractionated through a column (total reflux, variable take-off; 2·5 × 90 cm.; packed with 1/16" Dixon gauze rings). *trans*-3-Chlorotetrahydro-2-methylfuran (178 g., 27%), b. p. 129—131°, n_D^{20} 1·4412—1·4425, was collected, followed by an intermediate cut (32 g., 5%), and then the *cis*-isomer (278 g., 42%), b. p. 145—146°. (This last cut quickly darkened on storage.) Total yield, 74%; proportion of *trans*-isomer in product, 39% (Crombie *et al.*[2b, 5] report for the *trans*-isomer, b. p. 130°, n_D^{19} 1·4424, and for the *cis*, b. p. 147°, with 35% of *trans*-isomer in the product).

Pent-3-yn-1-ol.—*cis*-3-Chlorotetrahydro-2-methylfuran (121 g., 1·0 mole) was added dropwise during 30 min. to a stirred suspension of sodamide (from 80 g. of sodium and a catalytic quantity of ferric nitrate) in liquid ammonia (2·5 l.). After a further 15 hours' stirring, ammonium chloride (150 g.) was added, followed by sufficient water (*ca.* 500 c.c.) to give two clear phases. The product was continuously-extracted with ether, the dried ($MgSO_4$) solution evaporated, and the residue distilled, to give the required alkynol (46 g., 55%), b. p. 152—153°, n_D^{20} 1·4540. Crombie and Harper [30] report b. p. 154—157°, n_D^{20} 1·4554. Slightly lower yields (50%) were obtained in 0·4-mole runs.

cis-1-*Iodopent-3-ene.*—Pent-3-en-1-ol (44 g., 0·51 mole) (from pent-3-yn-1-ol by hydrogenation over Lindlar catalyst; cf. ref. 30) was added during 40 min. to a stirred slurry of toluene-*p*-sulphonyl chloride (108 g., 0·5 mole) in pyridine (53 c.c.) at 20° ± 2°. After a further 2 hours' stirring at room temperature the mixture was poured on ice, and the precipitated oil extracted with ether, washed with excess of 25% sulphuric acid, water, saturated aqueous sodium hydrogen carbonate, and water, and dried (K_2CO_3). Evaporation gave *cis*-pent-3-enyl toluene-*p*-sulphonate (110 g.). This, together with sodium iodide (77 g., 0·51 mole), was stirred in acetone (750 c.c.) under reflux for 2 hr. After cooling to 0°, the precipitated sodium toluene-*p*-sulphonate was filtered off and washed with ether, and the solvents were evaporated. The residue was washed with 10% aqueous sodium thiosulphate and water, dried ($MgSO_4$), and distilled, to yield *cis*-1-iodopent-3-ene (60 g., 67%), b. p. 53—55°/15 mm., n_D^{20} 1·5227. Goethals [31] records b. p. 53·6°/20 mm., n_D^{20} 1·5153. The *α-naphthalide* of *cis*-hex-4-enoic acid (prepared *via* the Grignard reagent) formed needles (from aqueous alcohol), m. p. 104—105° (Found: C, 80·2; H, 6·9; N, 5·7. $C_{16}H_{17}ON$ requires C, 80·3; H, 7·2; N, 5·85%).

trans-1-*Chloropent-3-ene.*—This halide, b. p. 108—109°, n_D^{20} 1·4360, was prepared in 75% yield from *trans*-pent-3-en-1-ol [25] as for tetrahydrofurfuryl chloride. Goethals [31] records b. p.

[29] Paul, *Ann. Chim.* (*France*), 1932, **18**, 338.
[30] Crombie and Harper, *J.*, 1950, 873.
[31] Goethals, *Bull. Soc. chim. belges*, 1937, **46**, 409.

107—107·5°/755 mm., n_D^{20} 1·4310, for 1-chloropent-3-ene. The *α-naphthalide* of *trans*-hex-4-enoic acid (prepared as above) formed needles (from aqueous alcohol), m. p. 134—135° (Found: C, 80·3; H, 7·1; N, 6·1%).

cis- *and* trans-*Hex-4-enoic Acid.*—These acids were prepared as for hex-5-enoic acid from *cis*-1-iodopent-3-ene (in 38% yield) and *trans*-1-chloropent-3-ene (in 68% yield) and had respectively: b. p. 112—113°/17 mm., n_D^{20} 1·4406 (*p*-bromophenacyl ester, m. p. 51—52°); b. p. 110—111°/17—18 mm., n_D^{20} 1·4385, m. p. −2° to +1° (*p*-bromophenacyl ester, m. p. 81—82°). Crombie and Harper [16] record for the *cis*-isomer, b. p. 106°/14 mm., n_D^{20} 1·4403 (*p*-bromophenacyl ester, m. p. 55°), and for the *trans*-isomer b. p. 108—109°/19 mm., m. p. −1° to +1°, n_D^{20} 1·4387 (*p*-bromophenacyl ester, m. p. 82·5°).

trans-6-*Bromohex-2-ene.*—Hex-4-en-1-ol [2a] (212 g., 2·12 moles) and pyridine (47 g., 0·60 mole) were added dropwise with stirring during 2 hr. to phosphorus tribromide (229 g., 0·85 mole) at −5°, then left at room temperature for 18 hr., after which volatile material (b. p. < 120°/20 mm.) was distilled off. The distillate was washed (water, 10% sodium carbonate solution, and water), dried ($MgSO_4$), and fractionally distilled, to yield *trans*-6-bromohex-2-ene (204 g., 59%), b. p. 48—51°/20 mm., n_D^{20} 1·4680 (Ansell and Selleck [32] found b. p. 42°/12 mm., n_D^{20} 1·4695), together with a dibromohexane (42 g., 15%), b. p. 97—98°/11 mm., n_D^{20} 1·5054 (Found: C, 29·7; H, 5·0. Calc. for $C_6H_{12}Br_2$: C, 29·5; H, 5·0%) (cf. 1 : 4-dibromohexane,[33] b. p. 98·2—98·4°/11—12 mm., $n_D^{15·5}$ 1·5084, and 1 : 5-dibromohexane,[34] b. p. 106—107°/15 mm., n_D^{15} 1·5072).

trans-6-*Chlorohex-2-ene.*—This *chloride*, b. p. 134—135°, n_D^{20} 1·4418, was prepared as for tetrahydrofurfuryl chloride, from *trans*-hex-4-en-1-ol in a 79% yield, on a 3-molar scale (Found: C, 61·2; H, 9·2. $C_6H_{11}Cl$ requires C, 60·7; H, 9·4%). The *α-naphthalide* of *trans*-hept-5-enoic acid (prepared *via* the Grignard reagent) formed felted needles (from aqueous alcohol), m. p. 89—90° (Found: C, 80·9; H, 7·7; N, 5·55. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·6; N, 5·5%).

trans-*Hept-5-enoic acid.*—This *acid*, b. p. 121—122°/17 mm., n_D^{20} 1·4424, was prepared as for hex-5-enoic acid from the preceding chloride in a 59% yield on a 1-molar scale (Found: C, 66·2; H, 9·5. Calc. for $C_7H_{12}O_2$: C, 65·6; H, 9·45%); Braun and Sobecki [14] give b. p. 117°/11 mm. Its p-*bromophenacyl ester*, plates (from aqueous alcohol), has m. p. 62—63° (Found: C, 55·6; H, 5·5. $C_{13}H_{17}O_3Br$ requires C, 55·4; H, 5·3%).

Ethyl trans-*Hex-4-enylmalonate.*—*trans*-6-Chlorohex-2-ene (166 g., 1·4 moles) was added during 30 min. to a warm, stirred solution of sodiomalonic ester [from ethyl malonate (216 g.) and sodium (30 g.) in alcohol (300 c.c.)], and the solution then stirred and boiled for 10 hr. After cooling, the precipitated salt was filtered off and washed with alcohol. Distillation of the combined alcoholic solutions gave *ethyl* trans-*hex-4-enylmalonate* (254 g. 75%), b. p. 143—144°/10 mm., n_D^{20} 1·4402 (Found: C 64·7; H, 9·3. $C_{13}H_{22}O_4$ requires C, 64·4; H, 9·15%).

trans-*Hex-4-enylmalonic Acid.*—The above ester (242 g., 1 mole) was added with stirring to a cold solution of potassium hydroxide (267 g.) in water (350 c.c.), followed by sufficient alcohol to produce homogeneity. After 24 hr. at room temperature the solution was cooled to 0° and made just acid to Congo-red with concentrated hydrochloric acid. The precipitated trans-*acid* was extracted with ether, the solvent removed, and the residual oil desiccated *in vacuo* over silica gel; it solidified. Crystallisation from benzene gave the pure acid (130 g., 70%), m. p. 115—116° (Found: C, 57·9; H, 7·3. $C_9H_{14}O_4$ requires C, 58·05; H, 7·6%).

trans-*Oct-6-enoic Acid.*—The above malonic acid (65 g., 0·35 mole) was decarboxylated at 150—160° for 5 hr. The product was dissolved in saturated sodium hydrogen carbonate solution and, after extraction with ether, the solution was acidified under light petroleum as described for hex-5-enoic acid. The final distillation gave trans-*oct-6-enoic acid* (42 g., 85%), b. p. 147—148°/23 mm., 74—76°/1 mm., n_D^{20} 1·4455 (Found: C, 67·3; H, 9·7. $C_8H_{14}O_2$ requires C, 67·6; H, 9·9). Its p-*bromophenacyl ester* formed plates (from alcohol), m. p. 70—71° (Found: C, 56·5; H, 5·4; Br, 23·8. $C_{16}H_{19}O_3Br$ requires C, 56·6; H, 5·7; Br, 23·6%), and the *phenylhydrazide* plates (from aqueous alcohol), m. p. 94—95° (Found: C, 72·7; H, 8·2; N, 11·9. $C_{14}H_{20}ON_2$ requires C, 72·4; H, 8·7; N, 12·1%).

3-*Chlorotetrahydro*-2 : 2-*dimethylfuran.*—A solution of 4 : 5-dihydro-2-methylfuran [21] (126 g., 1·5 moles) in ether (370 c.c.) was cooled to −60° and chlorine passed in until 103 g. (1·45 moles) were absorbed (*ca.* 45 min.). The resulting white solution was added from a cooled dropping funnel to a stirred solution of methylmagnesium bromide (from 45 g. of magnesium) in ether

[32] Ansell and Selleck, unpublished work.
[33] Glacét, *Compt. rend.*, 1944, **218**, 283.
[34] Paul, *Bull. Soc. chim. France*, 1938, **5**, 919.

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(1400 c.c.) at such a rate (*ca.* 30 min.) that gentle refluxing was maintained. The mixture was stirred for a further 15 min., then poured on crushed ice and ammonium chloride (43 g., 0·8 mole). On vigorous stirring two clear phases were obtained; the ethereal solution was separated and the aqueous layer extracted with ether. Distillation of the dried ($MgSO_4$) combined extracts gave 3-*chlorotetrahydro*-2 : 2-*dimethylfuran* (60 g., 30%), b. p. 47—49°/19 mm., n_D^{21} 1·4450 (Found: C, 53·8; H, 8·35; Cl, 26·6. $C_6H_{11}OCl$ requires C, 53·6; H, 8·2; Cl, 26·4%), and 3 : 3-*dichlorotetrahydro*-2 : 2-*dimethylfuran* (44 g., 17%), b. p. 88—89°/19 mm., n_D^{20} 1·4791 (Found: C, 43·3; H, 6·35. $C_6H_{10}OCl_2$ requires C, 43·6; H, 6·0%). The latter compound darkened slowly. Use of methylene chloride in the chlorination stage, or of an even larger excess of Grignard reagent in the coupling reaction, did not materially improve the yield or alter the relative amounts of the products.

3-*Bromotetrahydro*-2 : 2-*dimethylfuran*.—A stirred solution of 4 : 5-dihydro-2-methylfuran (152 g., 1·81 moles) in ether (400 c.c.) was cooled to −55° and treated dropwise with dry bromine until (after *ca.* 40 min.) flocks of solidified bromine remained undissolved. About 202 g. (1·30 moles) of bromine were thus used. The white suspension was added to methylmagnesium bromide and worked up, as for 3-chlorotetrahydro-2 : 2-dimethylfuran, to yield 3-*bromotetrahydro*-2 : 2-*dimethylfuran* (145 g., 45%), b. p. 58—60°/14 mm., n_D^{20} 1·4741 (Found: Br, 44·9. $C_6H_{11}OBr$ requires Br, 44·6%), and 3 : 3-dibromotetrahydro-2 : 2-dimethylfuran (95 g., 20%), b. p. 66—70°/0·3—0·5 mm. (too unstable to be obtained analytically pure).

4-*Methylpent*-3-*en*-1-*ol*.—A solution (50 c.c.) of 3-halogenotetrahydro-2 : 2-dimethylfuran (1·0 mole) in ether (500 c.c.) was added to a stirred suspension of sodium sand (51 g.) in ether (100 ml.). After a few minutes, reaction set in; the remainder of the solution was then added at such a rate that vigorous refluxing was maintained and the viscous mixture was stirred under reflux for a further 1 hr. Water was then added until two clear phases were obtained; the ethereal layer was separated, the aqueous phase extracted with ether, and the combined extracts were dried ($MgSO_4$) and fractionated, to give 85—87% yields of 4-methylpent-3-en-1-ol, b. p. 157—158° (62—63°/13 mm.), n_D^{19} 1·4452. Willimann and Schintz [35] give b. p. 98—100°/130 mm., n_D^{21} 1·4432; Bruylants and Dewael [36] give b. p. 157°, n_D^{20} 1·4455.

5-*Iodo*-2-*methylpent*-2-*ene*.—This *iodide* was prepared in 63—75% yield (0·5-molar scale) from 4-methylpent-3-en-1-ol *via* the toluene-*p*-sulphonate, as for *cis*-1-iodopent-3-ene. Distillation from silver powder gave a colourless product, b. p. 62—63°/13 mm., n_D^{17} 1·5246 (Found: C, 34·3; H, 5·5; I, 60·8. $C_6H_{11}I$ requires C, 34·3; H, 5·3; I, 60·4%). A compound ascribed this structure is reported [37] to have b. p. 176—180° (decomp.). The derived *thiuronium picrate*, yellow rhombs (from alcohol), had m. p. 136—137° (Found: C, 40·4; H, 4·7; N, 18·4. $C_{13}H_{17}O_7N_5S$ requires C, 40·3; H, 4·4; N, 18·1%). The α-*naphthalide* of 5-methylhex-4-enoic acid (prepared *via* the Grignard reagent) formed needles [from light petroleum (b. p. 100—120°)], m. p. 115—116° (Found: C, 80·2; H, 7·3; N, 5·9. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·6; N, 5·5%).

5-*Methylhex*-4-*enoic Acid*.—This *acid*, obtained in 61% yield (on 1-molar scale) from 5-iodo-2-methylpent-2-ene as for hex-5-enoic acid, had b. p. 98—99°/5 mm., m. p. −29° to −28°, n_D^{20} 1·4470. Linstead and Rydon [11] record b. p. 105°/5 mm., m. p. −33°, n_D^{30} 1·4461.

3-*Chlorotetrahydro*-2 : 2-*dimethylpyran*.—This *compound*, prepared in 38—45% yield (on a 1—2-molar scale) from 3 : 4-dihydro-6-methylpyran [22,24] as for 3-chlorotetrahydro-2 : 2-dimethylfuran, had b. p. 56—57°/10 mm., n_D^{20} 1·4606 (Found: C, 56·2; H, 9·0. $C_7H_{13}OCl$ requires C, 56·6; H, 8·8%). It was accompanied by a small amount of camphoraceous-smelling material of low b. p., which was halogen-free, saturated towards hydrogen in the presence of Adams catalyst, but decolorised bromine in carbon tetrachloride. A sample redistilled from sodium had b. p. 121—122°, n_D^{16} 1·4272 (Found: C, 73·7; H, 12·7. Calc. for $C_7H_{14}O$: C, 73·6; H, 12·4%). For tetrahydro-2 : 2-dimethylpyran Smith *et al.* [38] report b. p. 118—120°, n_D^{20} 1·4300.

3-*Bromotetrahydro*-2 : 2-*dimethylpyran*.—This *compound*, prepared in 55—61% yield (on a 1—2-molar scale) from 3 : 4-dihydro-6-methylpyran as for 3-bromotetrahydro-2 : 2-dimethylfuran, had b. p. 83—84°/20 mm., n_D^{20} 1·4884 (Found: Br, 41·9. $C_7H_{13}OBr$ requires Br, 42·4%).

[35] Willimann and Schintz, *Helv. Chim. Acta*, 1952, **35**, 2401.
[36] Bruylants and Dewael, *Bull. Sci. Acad. Roy. Belg.*, 1928, **14**, 140.
[37] Kishner and Klawikordow, *J. Russ. Phys. Chem. Soc.*, 1911, **43**, 595; *Chem. Zentr.*, 1911, **82**, 363; Favorskaya and Fridman, *J. Gen. Chem.* (*U.S.S.R.*), 1945, **15**, 421; *Chem. Abs.*, 1946, **40**, 4655.
[38] Smith, Norton, and Ballard, *J. Amer. Chem. Soc.*, 1951, **73**, 5273.

5-Methylhex-4-en-1-ol.—Ring scission of either 3-bromo- or 3-chloro-tetrahydro-2 : 2-dimethylpyran (1 mole) as for 3-chlorotetrahydro-2 : 2-dimethylfuran gave *5-methylhex-4-en-1-ol* (78—84%), b. p. 82—83°/20 mm., n_D^{18} 1·4520 (Found : C, 73·1; H, 12·3. $C_7H_{14}O$ requires C, 73·6; H, 12·4%). The *α-naphthylurethane* formed needles [from light petroleum (b. p. 80—100°)], m. p. 62—63° (Found : N, 5·2. $C_{18}H_{21}O_2N$ requires N, 4·9%).

2 : 6-Dichloro-2-methylhexane.—Treatment of 5-methylhex-4-en-1-ol (80 g., 0·4 mole) with thionyl chloride as for tetrahydrofurfuryl alcohol gave *2 : 6-dichloro-2-methylhexane* (72 g., 72%), b. p. 86—87°/15 mm., n_D^{20} 1·4539 (Found : C, 49·8; H, 8·50; Cl, 41·7. $C_7H_{14}Cl_2$ requires C, 49·7; H, 8·4; Cl, 41·9%). This compound gave an immediate precipitate when shaken with aqueous silver nitrate solution.

6-Iodo-2-methylhex-2-ene.—This *iodide*, prepared in 62—73% yield (0·5-molar scale) from 5-methylhex-4-en-1-ol as for *cis*-1-iodopent-3-ene, had b. p. 80—82°/13 mm., 50—52°/5 mm., n_D^{16} 1·5180 (Found : C, 37·4; H, 6·0; I, 57·2. $C_7H_{13}I$ requires C, 37·5; H, 5·9; I, 56·6%). The derived *thiuronium picrate* formed bright yellow laths (from alcohol), m. p. 138—139° (Found : C, 41·9; H, 4·9; N, 16·9. $C_{14}H_{19}O_7N_5S$ requires C, 41·9; H, 4·8; N, 17·4%). The *α-naphthalide* of 6-methylhept-5-enoic acid formed needles (from methyl alcohol), m. p. 117—118° (Found: N, 5·3. $C_{18}H_{21}ON$ requires N, 5·2%).

6-Methylhept-5-enoic Acid.—This *acid*, prepared in 36% yield from the preceding iodide (0·3 mole) as for hex-5-enoic acid, had b. p. 129—130°/12 mm., 88—92°/0·5—1 mm., n_D^{20} 1·4502 (Found : C, 67·4; H, 9·8. $C_8H_{14}O_2$ requires C, 67·6; H, 9·9%), and gave a p-*bromophenacyl ester*, plates (from alcohol), m. p. 50—51° (Found : C, 56·9; H, 5·8. $C_{16}H_{19}O_3Br$ requires C, 56·6; H, 5·7%), and a *phenylhydrazide*, plates (from alcohol), m. p. 84—85° (Found : C, 72·6; H, 8·4; N, 12·1. $C_{14}H_{20}ON_2$ requires C, 72·4; H, 8·7; N, 12·1%).

Ethyl 5-Methylhex-4-enylmalonate.—This *ester*, b. p. 144—145°/10 mm., n_D^{11} 1·4489, was prepared in 75% yield from 6-iodo-2-methylhex-2-ene (0·4 mole) as for ethyl *trans*-hex-4-enylmalonate (Found : C, 65·9; H, 9·5. $C_{14}H_{24}O_4$ requires C, 65·6; H, 9·4%).

5-Methylhex-4-enylmalonic Acid.—This *acid*, needles [from benzene–light petroleum (b. p. 40—60°)], m. p. 78—79°, was prepared in 69% yield from the corresponding ester (0·3 mole) as for *trans*-hex-4-enylmalonic acid (Found : C, 60·4; H, 8·1. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·05%).

7-Methyloct-6-enoic Acid.—This *acid*, b. p. 99—101°/0·7 mm., n_D^{20} 1·4513, was prepared in 84% yield from the above malonic acid (0·2 mole) as for *trans*-oct-6-enoic acid (Found : C, 69·1; H, 10·4. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%). Its *phenylhydrazide*, plates (from aqueous alcohol), had m. p. 87—88° (Found : C, 72·7; H, 8·75; N, 11·1. $C_{15}H_{22}ON_2$ requires C, 73·1; H, 9·0; N, 11·4%), and the p-*bromophenacyl ester* formed needles (from methanol), m. p. 56—57° (Found : C, 58·0; H, 6·4. $C_{17}H_{21}O_3Br$ requires C, 57·8; H, 6·0%).

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QUEEN MARY COLLEGE, UNIVERSITY OF LONDON,
MILE END ROAD, LONDON, E.1.

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338. *Solutions in Sulphuric Acid. Part XXI.* Conductivity Measurements on Some Nitro-compounds.*

By R. J. Gillespie and C. Solomons.

The behaviour of a number of nitro-compounds in sulphuric acid has been studied by measurements of the electrical conductivities of their solutions. The mononitro-compounds studied gave solutions whose conductivities increased with increasing concentration of the nitro-compound, and it was concluded that all these substances behave as weak bases. A method for determining the dissociation constants of weak bases from conductivity measurements on their solutions is described and applied to the mononitro-compounds. No evidence was obtained for the ionisation of any of the di- or tri-nitro-compounds, all of which depressed the conductivity of sulphuric acid: it was concluded that they are all non-electrolytes. Small differences in their behaviour have been tentatively interpreted in terms of solvation. Our results are compared with, and found to be generally in good agreement with, previous studies of solutions of nitro-compounds by ultraviolet spectroscopy and by cryoscopy. Cryoscopic measurements on two nitro-compounds not previously studied by this method are also reported.

Solutions of nitro-compounds in sulphuric acid have been studied by a number of workers, mainly by the cryoscopic method, although some electrical-conductivity and ultraviolet-spectroscopic measurements have also been made. The results and conclusions of different workers have not, however, always been in agreement. Thus, although it seems clear that nitrobenzene and various methyl- and halogen-substituted nitrobenzenes are weak bases, the extent of their ionisation has not been determined with any certainty. For nitromethane Hantzsch [1] concluded that it was un-ionised, but Gillespie [2] later believed his cryoscopic measurements to show that it was a weak base. There has also been disagreement concerning various aromatic polynitro-compounds, which have generally been assumed to be non-electrolytes, although Gillespie [2] concluded from cryoscopic measurements that 2 : 4 : 6-trinitrotoluene is a weak base. It has since been shown,[3] however, that the results of cryoscopic measurements on polynitro-compounds are difficult to interpret unambiguously.

It was the purpose of the present work to obtain further information about the behaviour of nitro-compounds in sulphuric acid by electrical-conductivity measurements. The electrical conductivities of solutions in 100% sulphuric acid of a series of mono- and poly-nitro-compounds were measured at 25° and at concentrations up to approximately 0·5 mole per kg. of soln. Some new measurements were also made on solutions of sulphuryl chloride, which is believed to be a non-electrolyte,[4] for comparison. Cryoscopic measurements on *p-tert.*-butylnitrobenzene and *p*-chloronitrobenzene are also reported and discussed.

The conductivity measurements are recorded in Tables 1 and 2 and Figs. 1 and 2, and the cryoscopic measurements in Tables 4 and 5.

On the basis of the conductivity measurements, the compounds studied fall into two groups: the mononitro-compounds in Table 1, which increase the conductivity of sulphuric acid; and the polynitro-compounds and sulphuryl chloride in Table 2, which decrease the conductivity of sulphuric acid.

Mononitro-compounds.—Since each of these substances gives a solution whose conductivity increases with increasing concentration, it is concluded that they are all ionised in sulphuric acid. The magnitudes of the conductivities of their solutions make it clear

* Part XX, *J.*, 1956, 3850.

[1] Hantzsch, *Z. phys. Chem.*, 1907, **61**, 257.
[2] Gillespie, *J.*, 1950, 2542.
[3] Brayford and Wyatt, *J.*, 1955, 3453.
[4] Gillespie, Hughes, and Ingold, *J.*, 1950, 2473.

TABLE 1. *Specific conductances of solutions of mononitro-compounds.*

Concn. (mole $kg._{soln.}^{-1}$)	κ (10^{-2} ohm^{-1} $cm.^{-1}$)	α	K_b	Concn. (mole $kg._{soln.}^{-1}$)	κ (10^{-2} ohm^{-1} $cm.^{-1}$)	α	K_b
Nitrobenzene				*p*-Chloronitrobenzene			
0·0391	1·092	0·363	0·0134	0·0215	1·051	0·209	0·0049
0·0766	1·158	0·270	0·0105	0·0430	1·062	0·192	0·0047
0·0989	1·212	0·257	0·0113	0·0861	1·090	0·163	0·0045
0·1284	1·251	0·224	0·0101	0·1486	1·130	0·124	0·0038
0·1936	1·369	0·199	0·0108	0·2289	1·174	0·097	0·0032
0·2186	1·386	0·182	0·0099				
0·2715	1·471	0·171	0·0108				
0·3073	1·487	0·153	0·0095				
0·3279	1·510	0·151	0·0096				
0·3997	1·588	0·139	0·0096				
0·4546	1·626	0·129	0·0092				
o-Nitrotoluene				*m*-Nitrotoluene			
0·0121	1·071	0·875	0·1477	0·0118	1·067	0·826	0·0973
0·0342	1·177	0·655	0·0562	0·0295	1·120	0·590	0·0373
0·0977	1·562	0·549	0·0698	0·0564	1·205	0·442	0·0251
0·1055	1·591	0·530	0·0671	0·0773	1·279	0·401	0·0247
0·1806	1·938	0·450	0·0686	0·1218	1·404	0·339	0·0236
0·1940	1·975	0·434	0·0663	0·1555	1·492	0·309	0·0233
0·2457	2·153	0·395	0·0647	0·2199	1·627	0·266	0·0224
0·2468	2·159	0·395	0·0650	0·2367	1·657	0·256	0·0220
0·3245	2·358	0·341	0·0579	0·2902	1·735	0·229	0·0206
0·3953	2·481	0·300	0·0513	0·3613	1·817	0·200	0·0188
p-Nitrotoluene				Nitromethane			
0·0172	1·101	0·896	0·2094	0·0330	1·051	0·136	0·0027
0·0536	1·342	0·678	0·0874	0·0589	1·056	0·109	0·0023
0·0780	1·527	0·652	0·1027	0·0869	1·069	0·117	0·0028
0·0804	1·521	0·627	0·0944	0·0935	1·067	0·104	0·0024
0·1556	1·985	0·546	0·1051	0·1523	1·105	0·104	0·0029
0·1634	2·000	0·525	0·0974	0·1664	1·094	0·087	0·0022
0·2297	2·303	0·459	0·0908	0·2414	1·145	0·082	0·0025
0·2440	2·338	0·455	0·0938	0·3337	1·195	0·072	0·0024
0·3044	2·530	0·340	0·0633				
0·3311	2·584	0·379	0·0773				
0·3439	2·746	0·403	0·0942				
0·3818	2·696	0·354	0·0746				
0·4825	2·834	0·302	0·0634				

TABLE 2. *Specific conductances of solutions of polynitro-compounds.*

Concn. (mole $kg._{soln.}^{-1}$)	κ (10^{-2} ohm^{-1} $cm.^{-1}$)	Concn. (mole $kg._{soln.}^{-1}$)	κ (10^{-2} ohm^{-1} $cm.^{-1}$)	Concn. (mole $kg._{soln.}^{-1}$)	κ (10^{-2} ohm^{-1} $cm.^{-1}$)	Concn. (mole $kg._{soln.}^{-1}$)	κ (10^{-2} ohm^{-1} $cm.^{-1}$)
o-Dinitrobenzene		*m*-Dinitrobenzene		2 : 4-Dinitrotoluene		2 : 4 : 6-Trinitrotoluene	
0·0225	1·023	0·1659	0·981	0·0429	1·025	0·0852	0·986
0·0402	1·024	0·1717	0·977	0·0726	1·024	0·1537	0·941
0·0845	1·004	0·2122	0·963	0·1207	0·992	0·2287	0·892
0·1005	0·996	0·2529	0·952	0·1771	0·970	0·3024	0·844
0·1461	0·976			0·2518	0·942	0·3712	0·801
0·1659	0·968	*p*-Dinitrobenzene					
0·2049	0·952	0·0210	1·035	1 : 3 : 5-Trinitrobenzene		Sulphuryl chloride	
0·2300	0·941	0·0399	1·031	0·0338	1·023	0·0101	1·041
0·2611	0·929	0·0657	1·015	0·0469	1·015	0·0115	1·041
0·3072	0·909	0·0834	1·013	0·0966	0·984	0·0317	1·034
0·3252	0·905	0·1107	0·998	0·1263	0·967	0·0460	1·031
0·3674	0·900	0·1244	0·997	0·1535	0·945	0·0629	1·026
0·3821	0·880	0·1607	0·981	0·1793	0·936	0·1051	1·016
		0·1869	0·972	0·2077	0·915	0·1370	1·006
m-Dinitrobenzene		0·2054	0·965	0·2421	0·899	0·1608	0·998
0·0134	1·038	0·2489	0·950	0·2871	0·868	0·2014	0·987
0·0398	1·027	0·2704	0·942	0·3032	0·863	0·2533	0·973
0·0529	1·024	0·3346	0·923	0·3576	0·826	0·2899	0·964
0·0599	1·020			0·3671	0·827	0·3018	0·961
0·0854	1·010	2 : 4-Dinitrotoluene				0·4234	0·928
0·1178	0·999	0·0125	1·038	2 : 4 : 6-Trinitrotoluene			
0·1269	0·994	0·0230	1·033	0·0336	1·021		

3 N

that they contain either the $H_3SO_4^+$ or the HSO_4^- ion,[5] and in accord with cryoscopic and spectroscopic evidence it is assumed that they ionise as simple bases according to the equation $R{\cdot}NO_2 + H_2SO_4 = R{\cdot}NO_2H^+ + HSO_4^-$. The order of decreasing conductivity of the solutions of these substances will be the order of decreasing base strength, which is therefore *p*- > *o*- > *m*-nitrotoluene > nitrobenzene > *p*-chloronitrobenzene > nitromethane. This order of base strengths agrees well with previous cryoscopic work [2] on nitrobenzene, *p*-nitrotoluene, and nitromethane, and with spectroscopic measurements [6] on *m*- and *p*-nitrotoluene, *p*-chloronitrobenzene, and nitrobenzene.

Dissociation Constants of Weak Bases from Conductivity Measurements.—The basic dissociation constant of a weak base, $K_b = [BH^+][HSO_4^-]/[B]$ can be written

$$K_b = [HSO_4^-]\alpha/(1 - \alpha) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where α is the degree of dissociation which can be obtained from conductivity measurements in the following manner. More than 97% of the current in a solution of any base

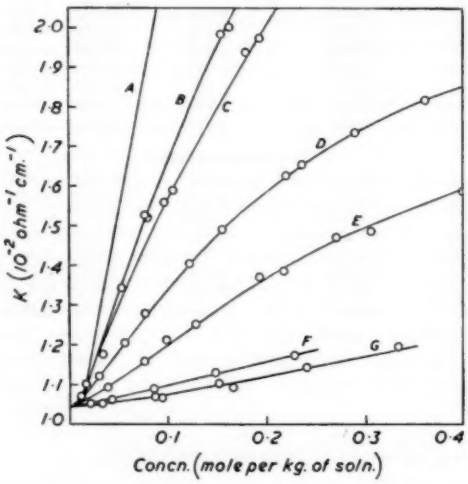

FIG. 1. *Specific conductances of solutions of mononitro-compounds.*

A, $KHSO_4$. *E*, $PhNO_2$.
B, *p*-$C_6H_4Me{\cdot}NO_2$. *F*, *p*-$C_6H_4Cl{\cdot}NO_2$.
C, *o*-$C_6H_4Me{\cdot}NO_2$. *G*, $MeNO_2$.
D, *m*-$C_6H_4Me{\cdot}NO_2$.

is carried by the hydrogen sulphate ion [7] and, therefore, in so far as we can ignore the slightly different effects of different cations on the molality of the hydrogen sulphate ion,[5] the concentration of the hydrogen sulphate ion in a solution of a weak base will be the same as that in a solution of a strong electrolyte having the same conductivity. Now, in a solution of a fully ionised univalent-metal hydrogen sulphate whose stoicheiometric concentration is c_s the concentration of hydrogen sulphate ion is given to a good approximation by

$$[HSO_4^-]_s = c_s/2 + \sqrt{(c_s^2/4 + K_{ap})} \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where K_{ap} is the autoprotolysis constant.[8] For a weak electrolyte whose stoicheiometric concentration is c_w the concentration of hydrogen sulphate ion is given by

$$[HSO_4^-]_w = \alpha c_w/2 + \sqrt{(\alpha^2 c_w^2/2 + K_{ap})} \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

For solutions of the same conductivity we have $[HSO_4]_s = [HSO_4^-]_w$, hence $\alpha = c_s/c_w$, and K_b may then be calculated from equation (1).

[5] Gillespie and Wasif, *J.*, 1953, 221.
[6] Brand, Horning, and Thornley, *J.*, 1952, 1374.
[7] Gillespie and Wasif, *J.*, 9153, 209.
[8] Gillespie, *J.*, 1950, 2516.

Dissociation Constants of Some Mononitro-compounds.—For the present calculations we have rather arbitrarily chosen potassium hydrogen sulphate as a reference strong electrolyte. This has the advantage that the conductivities of its solutions are very accurately known and that among the various fully ionised metal sulphates it exhibits an " average " behaviour.[5,9] The values of α and K_b for the various mononitro-compounds calculated as described above, K_{ap} (25°) being taken [10] as $2{\cdot}2 \times 10^4$, are given in Table 1. The values of K_b may be seen to be reasonably constant except in some cases at the lowest concentrations, when they seem to be abnormally high. This may reasonably be attributed to inaccuracies in the concentration of hydrogen sulphate ion as calculated from equation (2) at these low concentrations. These initial high values have been ignored in calculating the mean K_b values listed in Table 3.

TABLE 3. *Dissociation constants of some nitro-compounds.*

	K_b				K_b		
	Conduct.	Cryosc.	Spectr.		Conduct.	Cryosc.	Spectr.
p-tert.-Butylnitrobenzene	—	0·10	0·104	*m*-Nitrotoluene	0·023	—	0·024
p-Nitrotoluene	0·095	0·17 *	0·077	Nitrobenzene	0·010	0·025 *	0·009
o-Nitrotoluene	0·067	—	—	*p*-Chloronitrobenzene	0·004	0·003	0·0046
				Nitromethane	0·0025	0·004 *	—

* Taken from Part VII [2] and corrected for the change in the cryoscopic constant [11] from 5·98 to 6·12.

Cryoscopic Measurements.—Freezing-point depressions produced by *p-tert.*-butylnitrobenzene were measured in sulphuric acid containing a little acetone to repress the autoprotolysis; the results are given in Table 4. Row 3 of this table gives ν', the approximate value of the number of moles of particles produced in solution by one mole of the solute, calculated by means of the equation $\Delta\theta/m_2 = 6{\cdot}12\nu'(1 - 0{\cdot}001959\theta)[1 + (4m_2 + 12m_3)/9m_1]$ where m_1, m_2, and m_3 are the molalities of sulphuric acid, *p-tert.*-butylnitrobenzene, and acetone respectively, which is an extended and slightly modified form of equation 2 of Part XIX,[11] which allows for the presence of the second electrolyte acetone ($\nu_2 = 1{\cdot}5$, $s_2 = 1$, $\nu_3 = 2$, $s_3 = 2$; cf. equation 4 of Part I [4]). Since $\alpha = \nu' - 1$, where α is the degree of dissociation, the dissociation constant K_b is given by the expression

$$K_b = [(\nu' - 1)^2 m_2 + (\nu' - 1)m_3]/(2 - \nu')$$

Values of K_b thus calculated are given in Table 4, and the mean value is given in Table 3.

Freezing-point depressions produced by *p*-chloronitrobenzene were measured in 100% sulphuric acid, and the results are given in Table 5. Column 5 of this Table gives the values of ν' calculated by means of the equation $\theta/m_2 = 6{\cdot}12\nu'(1 - 0{\cdot}001959\theta)[1 + m_2/2m_1]$ which is the appropriate form of equation 2 of Part XIX.[11] Column 6 gives values of K_b calculated by means of the expression $K_b = (\nu' - 1)[HSO_4^-]/(2 - \nu')$, and the mean value is also given in Table 3. Values of K_b that have been obtained previously [2] by the cryoscopic method for *p*-nitroluene, nitrobenzene, and nitromethane are also given in Table 3.

TABLE 4. *Cryoscopic measurements on* p-tert.*-butylnitrobenzene.*

m_3	0·0000	0·0126	0·0348	0·0629	0·0914
$\Delta\theta$	—	0·122	0·328	0·570	0·814
ν'	—	1·62	1·57	1·50	1·47
K_b	—	0·12	0·11	0·09	0·09

Molality of acetone (m_3) = 0·0632.

Comparison of Dissociation Constants obtained by Different Methods.—Brand, Horning, and Thornley [6] measured the degree of dissociation at 18° of a number of nitro-compounds in slightly aqueous sulphuric acid and in oleum by means of their ultraviolet absorption spectra. They expressed their results in terms of pK_b values which are related to the

[9] Flowers and Gillespie, unpublished work.
[10] Gillespie and Solomons, unpublished work.
[11] Flowers, Gillespie, and Oubridge, *J.*, 1956, 1925.

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acidity function H_0 of the solvent by the relation $H_0 = pK_a + \log_{10}[B]/[BH^+]$ which we have converted into K_b values, for convenience of comparison, by means of the expression $\log K_b = pK_a - H_0 + \log [HSO_4^-]$. The value of H_0 and the corresponding value of the molality of the hydrogen sulphate ion $[HSO_4^-]$ were taken for 99·95% sulphuric acid. The value of $[HSO_4^-]$ was calculated from the expression $[HSO_4^-] = m/2 + \sqrt{\{(m/2)^2 + K_{ap}\}}$, where m is the molality of the water in the solvent and K_{ap} is the autoprotolysis constant,[8, 10] water being assumed to be fully ionised. The error introduced, if, as is likely, water is not quite completely ionised, is very small. These K_b values are given in the column headed " Spectr." in Table 3.

TABLE 5. *Cryoscopic measurements on* p-*chloronitrobenzene.*

m_2	F. p. (obs.)	F. p. (corr.)	θ	ν'	K_b	m_2	F. p. (obs.)	F. p. (corr.)	θ	ν'	K_b
0·0000	10·365°	10·515°	—	—	—	0·2079	9·031°	9·102°	1·413°	1·10	0·0030
0·0241	10·211	10·351	0·164°	—	—	0·2634	8·673	8·734	1·781	1·09	0·0031
0·0490	10·047	10·172	0·343	1·14	0·0024	0·3218	8·317	8·367	2·148	1·08	0·0031
0·0999	9·713	9·818	0·697	1·14	0·0029	0·3739	8·003	8·050	2·465	1·07	0·0031
0·1515	9·381	9·468	1·047	1·13	0·0033						

The values obtained from our conductivity measurements agree very well with the spectroscopic values, and the dissociation constants of the compounds listed in Table 3 may therefore be regarded as reasonably well established. It should be noted that the conductivity measurements were made at 25°, the spectroscopic measurements at approximately 18°, and the cryoscopic measurements at approximately 10°, but the effect of these relatively small temperature differences is almost certain, as pointed out by Brand, Horning, and Thornley,[6] to be negligible.

The values obtained by the cryoscopic method agree reasonably with the other values for *p-tert.*-butylnitrobenzene and *p*-chloronitrobenzene although they appear to be rather high for *p*-nitrotoluene, nitrobenzene, and nitromethane. It is noteworthy that the last three values are all earlier determinations in which water was added to repress the self-ionisation of the solvent. Brayford and Wyatt[3] recently showed that polynitro-compounds, which are non-electrolytes, give abnormally high freezing-point depressions in the presence of small amounts of water. Our results would be accounted for if mono-nitro-compounds exhibit the same behaviour in addition to a slight ionisation. The measurements on *p*-chloronitrobenzene were made in sulphuric acid containing no added electrolyte, and those on *p-tert.*-butylnitrobenzene in sulphuric acid containing a little acetone, and it appears from the work of Brayford and Wyatt that polynitro-compounds give normal depressions in the presence of acetone.

Effect of Substituents on the Basicity of Nitrobenzene.—It is most convenient to consider the effects of substituents in terms of the acidity constant of the conjugate acid of nitrobenzene $C_6H_5{\cdot}NO_2H^+$ which is inversely proportional to the basicity constant of nitrobenzene. The effects of some *meta*-substituents on the acidity constant have been satisfactorily accounted for by Brand, Horning, and Thornley[6] in terms of Kirkwood and Westheimer's theory[12] of the direct long-range electrostatic effect of substituent groups. Any interpretation of the effects of *ortho*- and *para*-substituents must, however, take into account the inductive and mesomeric effects. It may be noted that the conjugate acid of nitrobenzene is isoelectronic with benzoic acid, and the effects of substituents on their acid strengths might therefore be expected to be similar.

The strengths of the conjugate acids of nitrobenzene and the three nitrotoluenes are in the order H > *meta* > *ortho* > *para*, which, it is of interest, is intermediate between the order for the corresponding benzoic acids in water (*ortho* > H > *meta* > *para*) and the corresponding boronic acids in water (H > *meta* > *para* > *ortho*). Since the positive inductive effect of the methyl substituent is transmitted preferentially to the *ortho*- and

[12] Kirkwood and Westheimer, *J. Chem. Phys.*, 1938, **6**, 506, 513.

para-positions and more strongly to the *ortho*- than the *para*-position, we would on this basis alone expect the order found in the boronic acids. The anomalous position of the *ortho*-compound in the other two cases may be attributed to a steric effect [13] which appears therefore to be greater in *o*-toluic acid than in the conjugate acid of *o*-nitrotoluene. The effect of a *p-tert.*-butyl group in decreasing the acid strength is closely similar to, and perhaps a little greater than, that of a *p*-methyl group, as is also observed for the corresponding benzoic acids in water.

The effect of a *p*-chlorine atom in increasing the acid strength may be attributed to its negative inductive effect and is quantitatively similar to its effect on the strength of benzoic acid in water.

It is of interest that, whereas acetic acid is weaker than benzoic acid, the conjugate acid of nitromethane is stronger than that of nitrobenzene. This presumably indicates that the positive mesomeric effect of the phenyl group more than counteracts its negative inductive effect in the conjugate acid of nitrobenzene, whereas it does not do so in benzoic acid. It seems plausible that the positively charged nitrogen atom of the nitro-group should enhance the mesomeric effect of the phenyl group and also, because of its low polarisibility, hinder the transmission of the inductive effect of the phenyl group through to the oxygen atoms.

Reaction between Nitromethane and Sulphuric Acid.—Aromatic nitro-compounds appear to be stable in sulphuric acid, as the conductivities of their solutions remain unchanged after several days, but the conductivity of nitromethane solutions at 25° slowly increases and the colour of the solutions changes from pale yellow to deep yellow-brown. This reaction was not noticed during previous cryoscopic measurements,[2] probably because of the lower temperature, shorter duration, and lower accuracy of the measurements. In some recent work [3] a slight drift in the freezing points of solutions of nitromethane has been reported.

The change in the conductivity, approximately 5% after one hour, was not sufficient to cause a large error in the measurements if they were made during a few hours after the first addition of nitromethane, as were all the measurements reported in Table 1. We did not study this reaction any further, except to observe that pouring a sulphuric acid solution of nitromethane into water after it had been allowed to react for some hours gave a strongly reducing solution (probably containing hydroxylamine) and a combustible gas (probably carbon monoxide). These observations are consistent with previous work on the reaction between aliphatic nitro-compounds and mineral acids.[14]

Polynitro-compounds.—All the polynitro-compounds that we investigated decrease the conductivity of sulphuric acid (Table 2; Fig. 2). We conclude that our conductivity measurements give no evidence for the ionisation of any of these solutes. The conductivity of their solutions must be attributed to the ions resulting from the self-dissociation of the solvent.

The diminution in the conductivity of sulphuric acid caused by these solutes must be due to their decreasing either the concentration of the self-dissociation ions or the mobilities of these ions, or to both these effects. The concentrations of the self-dissociation ions will be reduced because of the dilution of the solvent by the added solute, and would be further reduced if the solute is solvated. Changes in various properties of the solution, such as its dielectric constant, caused by the presence of the solute may also be contributing factors in reducing the concentrations of the self-dissociation ions. The extent to which the solute will affect the mobilities of the ions is difficult to predict, but any disruption of the structure of the liquid, which is liable to be considerable if solvation occurs, is likely to be accompanied by a decrease in the mobilities of the ions. Metal cations, which are believed to be solvated,[15] are known to reduce the mobility of the hydrogen sulphate ion [5] and they

[13] See, *e.g.*, Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 743.
[14] Hass and Riley, *Chem. Rev.*, 1943, **3**, 371.
[15] Gillespie and Oubridge, *J.*, 1956, 80.

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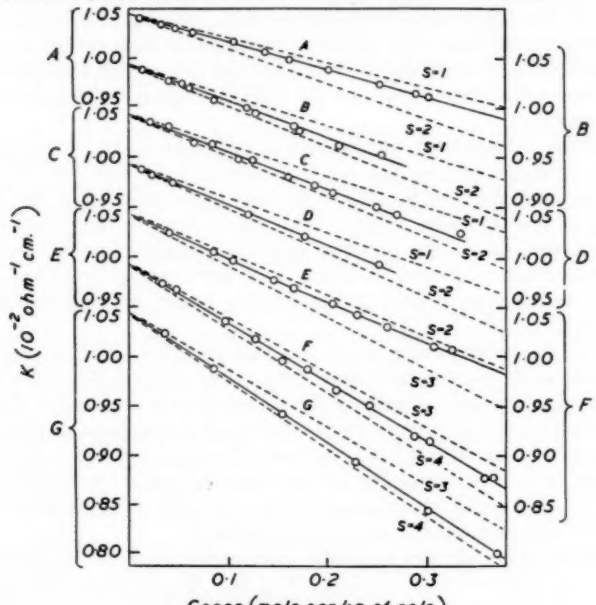
probably also reduce the mobility of the hydrogen ion ($H_3SO_4^+$). In the following discussion we shall consider only the ions resulting from the autoprotolysis and ignore those resulting from the self-dehydration, since the concentrations of the former are greater [8] and their mobilities are very much greater.[5] Our results can be treated quantitatively if only the dilution and solvation effects on the concentration of the autoprotolysis ions are considered, and other effects, such as those due, for example, to the changing dielectric constant of the solvent, are ignored, and if it is also assumed that the mobilities of the autoprotolysis ions remain constant. It then follows that the conductivity of the solution is proportional to the molar concentration of "free" solvent in the solution, *i.e.*, $\kappa/\kappa_0 = c_1/c_0 = (1000d - c_2M_2 - c_2sM_1)/1000d_0$, where c_1 is the molar concentration of the solvent in the solution, c_0 is the molar concentration of the solvent in the pure

FIG. 2. *Specific conductances of solutions of polynitro-compounds.*



A, SO_2Cl_2.
B, *m*-$C_6H_4(NO_2)_2$.
C, *p*-$C_6H_4(NO_2)_2$.
D, 2 : 4-$C_6H_3Me(NO_2)_2$.
E, *o*-$C_6H_4(NO_2)_2$.
F, 1 : 3 : 5-$C_6H_3(NO_2)_3$.
G, 2 : 4 : 6-$C_6H_2Me(NO_2)_3$.

solvent, and M_1 is its molecular weight, c_2 is the molar concentration of the solute and M_2 is its molecular weight, s is the solvation number of the solute, d_0 is the density of the solution, κ_0 is the conductivity of the pure solvent, and κ the conductivity of the solution. It will be convenient if we convert molar concentrations (c) into units (ω) of mole per kg. of solution [17] ($c = \omega d$), then we obtain $\kappa = \kappa_0 d\omega(1 - 10^{-3}M_2 - 10^{-3}sM_1)/d_0$. The densities of the solutions were measured and they may with sufficient accuracy be expressed as linear functions of the concentration, $d = d_0(1 - a\omega)$ where a has the following values: *o*-dinitrobenzene 0·086, *m*-dinitrobenzene 0·078, *p*-dinitrobenzene 0·080, 2 : 4-dinitrotoluene 0·108, 1 : 3 : 5-trinitrobenzene 0·036, 2 : 4 : 6-trinitrotoluene 0·066. Values of κ at various concentrations were calculated for each of the solutes for various solvation numbers s. They have been plotted against concentration in Fig. 2, where they may be compared with th experimental results. The solvation numbers giving approximately the best agreement with the experimental results are listed in Table 6.

TABLE 6. *Solvation numbers of polynitro-compounds.*

	Solvation number	s/n *		Solvation number	s/n *
o-Dinitrobenzene	2·1	1·1	1 : 3 : 5-Trinitrobenzene ...	3·5	1·2
m-Dinitrobenzene	1·6	0·8	2 : 4 : 6-Trinitrotoluene	3·7	1·2
p-Dinitrobenzene	1·7	0·9	(Sulphuryl chloride)	1·3	—
2 : 4-Dinitrotoluene	1·7	0·9			

* n is the number of nitro-groups in the molecule.

In view of the fact that mononitro-compounds are partly ionised in sulphuric acid, and other evidence [16] that if it is not protonated the nitro-group tends to form hydrogen bonds with a sulphuric acid molecule, it seems reasonable to suppose that solvation occurs largely by formation of hydrogen bonds between sulphuric acid molecules and nitro-groups. It is therefore of interest that s/n, the ratio of the total solvation number to the number of nitro-groups, has a constant value of approximately unity (Table 6).

It should perhaps be pointed out that some of the differences in the depressions of the conductivity caused by different nitro-compounds could conceivably be due to very small but different amounts of ionisation, insufficient to increase the conductivity enough to overcome the decrease caused by solvation and other effects. If, however, we accept the cryoscopic evidence that sulphuryl chloride is a non-electrolyte,[4] it seems unlikely that the polynitro-compounds, which depress the conductivity more than does sulphuryl chloride, can be even slightly ionised.

We may conclude that our conductivity measurements show that it is unlikely that the polynitro-compounds that we have investigated are ionised at all, and that if they are the degree of their ionisation must be very small. Our conclusions are in agreement with those of Brand, Horning, and Thornley [6] from their spectroscopic measurements. It is noteworthy that these authors pointed out that Gillespie's cryoscopic results [2] on 2 : 4 : 6-trinitrotoluene, from which he concluded that it was ionised, could alternatively be accounted for if it was assigned a solvation number of four, which is close to the value that we have calculated above from our conductivity results. This agreement may, however, be fortuitous, since Gillespie's measurements were made in sulphuric acid containing a little water, and Brayford and Wyatt [3] have recently shown that polynitro-compounds give quite appreciably differing freezing-point depressions in sulphuric acid containing small amounts of various different electrolytes, including water, which cannot be satisfactorily accounted for in terms of solvation.

EXPERIMENTAL

Apparatus.—The conductivity bridge and cells, and the general procedure for making the conductivity measurements, are described elsewhere.[17] Densities of solutions were measured with a specific-gravity bottle.

Materials.—Sulphuric acid was prepared and adjusted to the composition 100% H_2SO_4 by means of its conductivity as described elsewhere.[17]

Liquid solutes were dried and redistilled and had the following b. p.s : nitromethane 100·3—100·5°; nitrobenzene 207°; *o*-nitrotoluene 218°; *m*-nitrotoluene 228°. The solid solutes were recrystallised several times, and then dried in an oven. All solutes were stored in stoppered bottles in desiccators over phosphoric oxide.

We thank the London County Council for the award of a Major County Scholarship (to C. S.), Dr. J. A. Leisten who made the cryoscopic measurements on *p-tert.*-butylnitrobenzene, Dr. J. V. Oubridge who made the cryoscopic measurements on *p*-chloronitrobenzene, and Mr. R. Flowers who made the density measurements.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, COWER ST., LONDON, W.C.1. [*Received, September 12th,* 1956.]

[16] Gillespie and Millen, *Quart. Rev.*, 1948, **2**, 277.
[17] Gillespie, Oubridge, and Solomons, following paper.

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339. *Solutions in Sulphuric Acid. Part XXII.* A Reinvestigation of the Electrical Conductivity of the Water–Sulphur Trioxide System, with Special Reference to the Composition of Minimum Conductivity.*

By R. J. Gillespie, J. V. Oubridge, and C. Solomons.

The electrical conductivity of the water–sulphur trioxide system in the region of the composition H_2SO_4 has been reinvestigated. The values of the minimum conductivity and the composition at which it occurs have been determined at 10°, 25°, and 40° from experiments in which the electrical conductivity and the freezing point of the same solution in a combined conductivity cell and cryoscope were measured over a range of compositions in the neighbourhood of the composition H_2SO_4. New values are given for the conductivities of solutions of water and sulphur trioxide in sulphuric acid.

In a previous investigation [1] of the electrical conductivity of the water–sulphur trioxide system in the neighbourhood of the composition H_2SO_4 it was found that at 25° the minimum conductivity occurs at the composition H_2SO_4 to within ± 0.003m (H_2O or $H_2S_2O_7$). At the freezing point of sulphuric acid (10·37°), Kunzler and Giauque [2] found that the minimum conductivity did not occur exactly at the composition H_2SO_4 but at 99·996 $\pm$ 0·001 weight % (*i.e.*, 0·002 $\pm$ 0·0005 mole of H_2O per kg. of solution). It was subsequently stated by Kunzler [3] that the composition of minimum conductivity changes by less than 0·003 weight % (*i.e.*, 0·0015 mole per kg. of solution) over the range 5—20°. It will be shown in a later paper that the exact position of minimum conductivity is of considerable importance in connection with the determination of the mobilities of the $H_3SO_4^+$ and HSO_4^- ions in sulphuric acid, and a knowledge of these mobilities is essential for an understanding of the mechanism of chain-conductance in sulphuric acid. Since neither Kunzler and Giauque [2] nor Kunzler [3] made any measurements at 25°, or gave actual conductivity values † at any temperature, we considered it worth while to repeat our earlier measurements at 25° with greater accuracy and to extend them to other temperatures. In order to achieve the accuracy necessary for this work and other work on the conductivities of solutions in sulphuric acid (see, *e.g.*, refs. 27 and 28), the conductivity bridge and cells used previously [1] were replaced by apparatus of considerably improved design.

Experimental

Conductance Bridge.—This consisted of an A.C. Wheatstone bridge network with a resistance–capacitance Wagner earth, the design being based on Luder's [4] precision bridge circuit. The resistance boxes used as standards were non-inductive 5-decade boxes (Doran Instrument Co. and Croydon Precision Instrument Co.) reading to 11,111 ohms in 0·1 ohm steps. They were calibrated by the method of self-comparison with an accuracy of 0·02%. For most measurements the bridge was supplied with 1000 c./sec. A.C. of pure sinusoidal-waveform at an input voltage of 0·8—1·0 v r.m.s. For tests of electrode polarisation a multi-frequency oscillator giving 300 to 10,000 c./sec. was used. The out-of-balance voltage from the bridge was fed into a two-stage audio-frequency amplifier [4] and was detected in sensitive headphones. With this apparatus and the use of the "separate terminal balance" method [4] a sharp balance point to 0·1 ohm in more than 10,000 ohms could be obtained.

Thermostats.—For an accuracy of 0·01% in the measurement of the resistance of sulphuric acid, which has a temperature coefficient [2] of approximately 4% per °c the temperature must be controlled to better than $\pm 0.003°$. The thermostats used were lagged copper tanks, each

* Part XXI, preceding paper.

† These authors measured the variation of the resistance of sulphuric acid with change of composition in a cell of unknown cell constant.

[1] Gillespie and Wasif, *J.*, 1953, 204.
[2] Kunzler and Giauque, *J. Amer. Chem. Soc.*, 1952, **74**, 804.
[3] Kunzler, *Analyt. Chem.*, 1953, **25**, 93.
[4] Luder, *J. Amer. Chem. Soc.*, 1940, **62**, 89.

holding 15 gallons of Shell " Diala-B " transformer oil and equipped with an efficient stirrer and a mercury–toluene regulator. The temperatures were set by comparison with thermometers calibrated by the National Physical Laboratory. The absolute accuracy of their calibrations was ±0·005°, corresponding to an error of 0·02% in the absolute values of specific conductance. For the 25° tank the temperature was controlled by a T41 gas-filled triode and mercury–toluene regulator and remained constant to within ±0·002°. The thermostats at 10° and 40° were regulated within ±0·01° by " Sunvic " hot-wire vacuum switches. The 10° tank was also fitted with a commercial refrigerator unit.

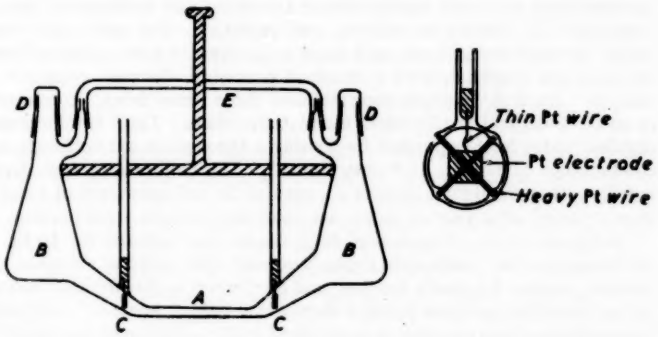

FIG. 1. *Conductivity cell I.*

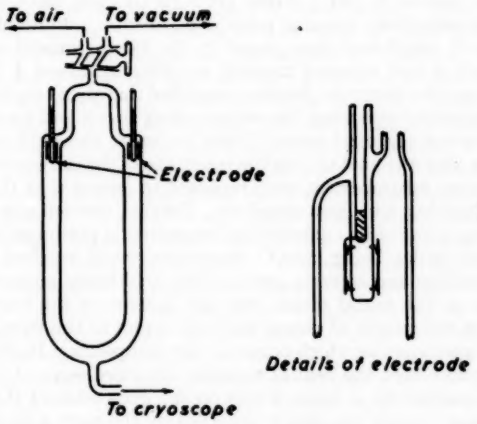

FIG. 2. *Conductivity cell II.*

Conductivity Cells.—These were of " Pyrex " glass with pinch-sealed platinum electrodes. Some of the earlier measurements were made with the cells used previously by Gillespie and Wasif.[1] The electrode chamber of this type of cell was filled by a pressure of dry air. Most of the measurements were, however, carried out in cells of a new design which avoids the use of air pressure. In these cells (Fig. 1) the electrode chamber (*A*) joins the two flasks (*B*) which act as a reservoir, and it is therefore washed out each time the solution is poured from one flask to the other by tilting the cell. The solution is easily mixed after the addition of solute by repeatedly running the solution from one flask to the other by tilting. The electrodes (*C*) were attached rigidly to the sides of the cell by stout platinum wires as shown in Fig. 1. The mixing of the cell contents is facilitated when the cell is tilted because of the turbulent motion set up around the electrodes.

For experiments in which the freezing point and the conductivity of the same sample of solution were measured a combined cryoscope–conductivity cell was used. The conductivity

cell (Fig. 2) was U-shaped and communicated with the cryoscope [5] at its lower end. It was attached close to the side of the cryoscope. The size and shape of this cell were largely dictated by the necessity of being able to insert the whole combined cell into a suitable air-jacket for the freezing-point measurements. The cell was filled from the cryoscope, which acts as a reservoir, by means of suction applied through the two-way tap.

Great care was taken in the construction of the cells to eliminate all pinholes in the glass. In agreement with the earlier findings by Trenner and Taylor,[6] and contrary to the practice of some other workers,[7] conditioning of the electrodes, by electrodeposition of platinum black, was found to be necessary to eliminate electrode polarisation resistances. The platinising solution used was that recommended by Jones and Bollinger.[8] New electrodes were plated, " greyed " by heating to redness, and replated. The cells were then washed with distilled water, steamed for an hour, and dried in an oven at 120°. The cells were calibrated by means of Jones and Bradshaw's 0·1 D standard potassium chloride solution.[9] The potassium chloride was an " AnalaR " sample recrystallised three times from " conductance " water, then dried in an air-oven, and finally fused in a platinum dish. The " conductance " water was laboratory distilled water further purified by passing it through an ion-exchange column. It had a specific conductance of $1—2 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$. The calibrations were reproducible to better than 0·05%, although slightly greater changes in the cell constants of some of the cells were noticed over a period of a year or more, necessitating periodic recalibration.

Sulphuric Acid.—Commercial 65% oleum was refluxed for 10 hr. with chromium trioxide to decompose any oxidisable impurities, and then sulphur trioxide was distilled off at atmospheric pressure by gently heating, and condensed as the liquid at room temperature. This was twice redistilled and then distilled slowly into 98% " AnalaR " sulphuric acid, to form a concentrated oleum which was diluted as required by the addition of water or 98% " AnalaR " acid. All the samples of acid whose freezing points were measured had maximum freezing points above 10·361° in good agreement with the value of 10·365 ± 0·005° given by Gillespie and Oubridge.[10]

Procedure.—For the combined conductivity–freezing point experiments, a dilute oleum was weighed into the cell shown in Fig. 2, which was then placed in the 25° thermostat with continuous stirring of its contents until it had attained thermal equilibrium (about ½ hr.). By applying a slight pressure with dry air the electrode chamber was filled and then emptied again. The solution in the cryoscope was mixed by operating the reciprocating stirrer and the electrode chamber was refilled. This process was repeated several times to ensure thorough mixing of the solution. Ten to fifteen minutes after the final mixing the resistance of the cell was measured, then the mixing process and resistance measurement were repeated to ensure that the mixing and the washing of the electrode chamber had been complete. Finally, the cell was removed from the thermostat and the freezing point of its contents was measured, a platinum resistance thermometer and Smith's difference bridge being used.[5] Successive small weighed amounts of water were then added, the resistance and freezing point of the acid being measured after each addition. The concentration of the initial oleum was not known at the start of the experiment, but was calculated from the weight of oleum used and a plot of the freezing point against weight of water added, the maximum of which occurs at the composition H_2SO_4.

In experiments in which water was added the heat of reaction vaporised some of the water which then condensed on, or was absorbed by, a layer of acid on the glass walls of the cell out of contact with the liquid. The " lost " water was slowly absorbed by the surface layer of acid in the cell, with the result that a small change of conductivity took place each time the cell was shaken. Because of such drifts, the experiments in which water was added were rather tedious, the solutions often taking several hours to become homogeneous after each addition. Therefore, most experiments were carried out by adding water as a dilute solution in sulphuric acid, when, as the heat of solution was much smaller, no appreciable amount of water was vaporised and no drifts were observed. As the exact concentration of the aqueous acid added in these experiments was not known at the start of the experiment, a plot of the conductivities and concentrations obtained from the experiments in which water was added was used to determine the compositions of two solutions in the aqueous acid experiments. From a knowledge of the

[5] Gillespie, Hughes, and Ingold, *J.*, 1950, 2473.
[6] Trenner and Taylor, *J. Phys. Chem.*, 1931, **35**, 1336.
[7] *E.g.*, Brand, Horning, and Thornley, *J.*, 1952, 1374.
[8] Jones and Bollinger, *J. Amer. Chem. Soc.*, 1935, **57**, 280.
[9] Jones and Bradshaw, *J. Amer. Chem. Soc.*, 1933, **55**, 1780.
[10] Gillespie and Oubridge, *J.*, 1956, 80.

amount of aqueous acid added between these two compositions the concentration of the water in the aqueous acid was found, and the compositions of the other solutions were then calculated.

Once the conductivity of 100% sulphuric acid had been determined from experiments in which both the conductivity and the freezing point were measured, further experiments were carried out in which only conductivity was measured in cells of the type shown in Fig. 1. The compositions of the solutions were calculated as above from the initial weight of oleum taken and the weights of water or aqueous acid added, the conductivity of 100% acid being used instead of the maximum freezing point as the reference point.

The effect of temperature on the conductivity of the water–sulphur trioxide system was studied in experiments in which the composition was varied by the addition of aqueous acid. The conductivity of each solution was determined at 9·66°, 25°, and 40°, and its composition was found from the plot of the conductivity at 25° against composition obtained from previous experiments.

Results.

For purposes of discussion and comparison the results of conductivity measurements are generally most conveniently expressed in volume concentration units such as molarity or normality. Our solutions could not be made up with sufficient accuracy by volume and they were all made up by weight. In order to express the concentrations of the solutions in volume concentration units it is necessary to know their densities, but in the case of sulphuric acid solutions these are in many cases not known, or are not known with sufficient accuracy. We have found that it is generally most convenient to express our concentrations as moles of solute per kg. of solution (moles $kg._{soln.}^{-1}$). This unit is not widely used and has no special name or symbol, although these would be useful, but it appears to have several advantages. Concentrations in molar units are simply obtained from concentrations in moles $kg._{soln.}^{-1}$ units by multiplying the latter by the density of the solution. Many workers have attempted to avoid the difficulty caused by the lack of knowledge of densities of solutions by using instead the density of the solvent to give an approximate or " pseudo " molarity, but since they are often not careful to distinguish between this quantity and the true molarity, confusion is liable to arise. Mole-fractions and molalities suffer from the disadvantage that they can have more than one value in cases, for example, where the solute is dissociated, reacts with, or is solvated by, the solvent. Thus one can calculate a stoicheiometric molality on the assumption that the solute dissolves unchanged, or various " true " molalities depending on the particular assumptions made concerning the internal state of the system. Volume concentration units such as molarities do not have this disadvantage, but they are, on the other hand, temperature dependent, and have the disadvantage that a given molecular concentration has a different molarity at different temperatures. Concentrations expressed in mole $kg._{soln.}^{-1}$ units are, however, independent of any assumptions concerning the internal state of the system, and they are also independent of temperature. Concentrations of oleums (*i.e.*, solutions of sulphur trioxide in sulphuric acid) are expressed in terms of disulphuric acid $H_2S_2O_7$ as this is the predominant species in the dilute oleums with which we are concerned.

It is not possible to give in detail the results of all the very large number of measurements that were made. The results of our measurements over the concentration range 0·015 mole of $H_2S_2O_7$ $kg._{soln.}^{-1}$ to 0·015 mole of H_2O $kg._{soln.}^{-1}$ are shown in Fig. 3. The freezing points agree very well with the previous work of Kunzler and Giauque [2] and they serve to determine the position of the composition H_2SO_4 to better than 0·0005 mole $kg._{soln.}^{-1}$. It can be seen that the minimum conductivity occurs on the aqueous side of the composition H_2SO_4. From a large-scale version of this plot it was concluded that the minimum value of the specific conductance at 25° of $(1{\cdot}0432 \pm 0{\cdot}0005) \times 10^{-2}$ ohm^{-1} $cm.^{-1}$ occurs at a concentration of $0{\cdot}0019 \pm 0{\cdot}0005$ mole $kg._{soln.}^{-1}$, and that at the composition H_2SO_4 the specific conductance is $(1{\cdot}0439 \pm 0{\cdot}0005) \times 10^{-2}$ ohm^{-1} $cm.^{-1}$ (Table 3). The results of the conductivity measurements at 25° over the concentration range 0·15 mole of $H_2S_2O_7$ $kg._{soln.}^{-1}$ to 0·1 mole of H_2O $kg._{soln.}^{-1}$ are shown in Fig. 4. From large-scale versions of the plots shown in Figs. 3 and 4, and others covering a wider concentration range, values of the specific conductance at round concentrations were interpolated. These are given in Tables 1 and 2. Interpolated values obtained from the measurements made at 9·66° and 40·00° are also given in Table 1. The values at 9·66° and at 40·00° of the composition of minimum conductivity and the specific conductances at these compositions and at the composition H_2SO_4 are given in Table 3. The accuracy of the results

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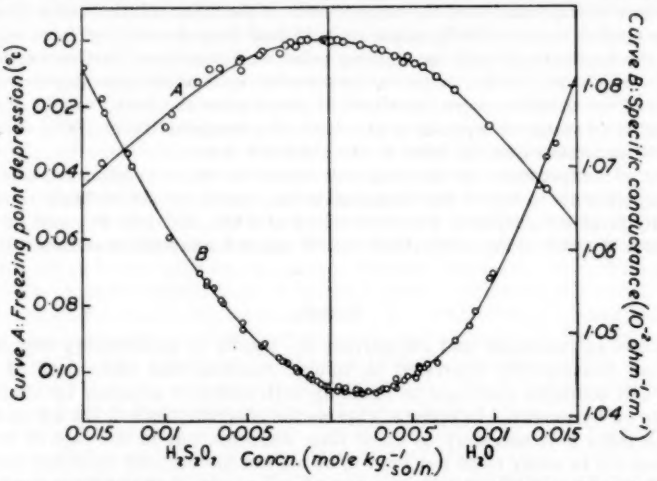
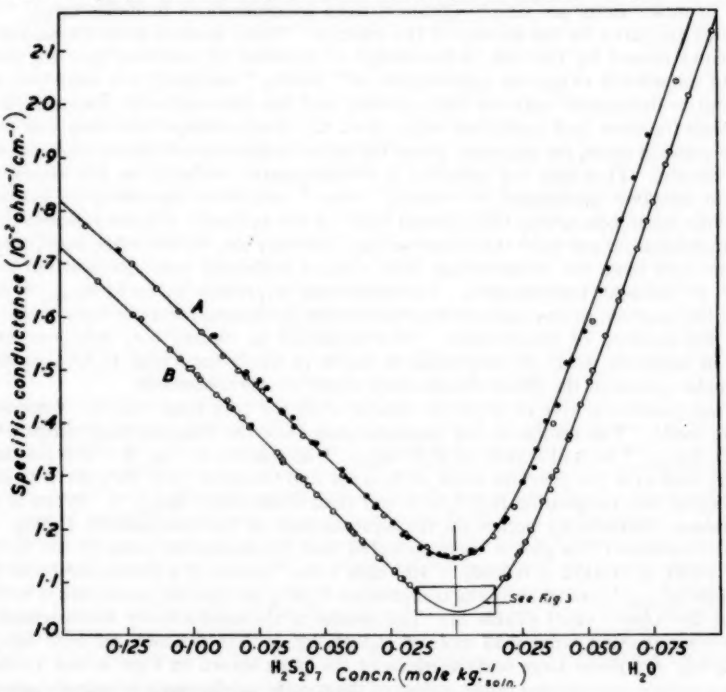
FIG. 3. *Freezing points and conductances in the region of the composition* H_2SO_4.



Curve *A* : Freezing-point depression (°c). Curve *B* : Specific conductance (10^{-2} ohm^{-1} cm.$^{-1}$).

FIG. 4. *Specific conductance of dilute solutions of* H_2O *and* $H_2S_2O_7$ *in sulphuric acid.*



A { ○ Hetherington, Hub, Nichols, and Robinson (see ref. 24).
● Gillespie and Wasif.
—— Mean curve of present work shifted vertically by 0·1 (10^{-2} ohm^{-1} cm.$^{-1}$) and horizontally to the left by 0·0019 (mole kg.$_{soln.}^{-1}$).

B { ○ Experimental points. } Present work.
—— Mean curve. }

at these temperatures is not as great as at 25° because of the fewer measurements made and because the temperatures of the thermostats were less accurately controlled.

TABLE 1. *Interpolated specific conductances* (10^{-2} *ohm*$^{-1}$ *cm.*$^{-1}$) *at low concentration at* 9·66°, 25·00°, *and* 40·00°.

Concn.	$H_2S_2O_7$			H_2O		
(mole kg.$_{soln.}^{-1}$)	9·66°	25·00°	40·00°	9·66°	25·00°	40·00°
0·000	0·5700	1·0439	1·7106	0·5700	1·0439	1·7106
0·001	0·5713	1·0447	1·7111	0·5690	1·0436	1·7103
0·002	0·5730	1·0459	1·7117	0·5685	1·0432	1·7103
0·003	0·5751	1·0473	1·7125	0·5686	1·0437	1·7105
0·004	0·5772	1·0489	1·7140	0·5691	1·0440	1·7109
0·005	0·5794	1·0506	1·715	0·5699	1·0453	1·712
0·006	0·5819	1·0530	1·717	0·5711	1·0467	1·713
0·007	0·5845	1·0554	1·718	0·5725	1·0483	1·715
0·008	0·5870	1·0579	1·722	0·5741	1·0505	1·717
0·009	0·5896	1·0608	1·724	0·5759	1·0533	1·719
0·010	0·5921	1·0639	1·727	0·5783	1·0570	1·723
0·012	0·5975	1·0709	1·734	0·5845	1·0658	1·731
0·014	0·6028	1·0783	1·742	0·5931	1·0761	1·742
0·016	0·6081	1·0861	1·750	0·6035	1·0876	1·756
0·018	0·6135	1·0942	1·759	0·6164	1·0994	1·774
0·020	0·619	1·102	1·769	0·632	1·112	1·793
0·030	0·652	1·148	1·821	0·717	1·208	—
0·040	0·687	1·199	1·878	—	1·327	—
0·050	0·727	1·251	1·940	—	1·453	—

TABLE 2. *Interpolated specific conductances* (10^{-2} *ohm*$^{-1}$ *cm.*$^{-1}$) *at higher concentrations at* 25·00°.

Concn. (mole kg.$_{soln.}^{-1}$)	$H_2S_2O_7$	H_2O	Concn. (mole kg.$_{soln.}^{-1}$)	$H_2S_2O_7$	H_2O	Concn. (mole kg.$_{soln.}^{-1}$)	$H_2S_2O_7$	H_2O	Concn. (mole kg.$_{soln.}^{-1}$)	$H_2S_2O_7$	H_2O
0·00	1·044	1·044	0·07	1·351	1·733	0·18	1·844	3·180	0·32	2·32	4·64
0·01	1·064	1·057	0·08	1·400	1·875	0·20	1·918	3·419	0·34	2·39	4·82
0·02	1·102	1·112	0·09	1·448	2·017	0·22	1·99	3·64	0·36	2·45	4·99
0·03	1·148	1·208	0·10	1·496	2·160	0·24	2·06	3·86	0·38	2·51	5·15
0·04	1·199	1·327	0·12	1·593	2·430	0·26	2·13	4·07	0·40	2·58	5·30
0·05	1·251	1·453	0·14	1·682	2·689	0·28	2·19	4·27	0·42	—	5·46
0·06	1·303	1·592	0·16	1·766	2·940	0·30	2·26	4·46	0·44	—	5·60

TABLE 3. *Specific conductances at the composition* H_2SO_4 *and at the composition of minimum conductance.*

Temp.	κ (10^{-2} ohm^{-1} cm.$^{-1}$) H_2SO_4	κ (10^{-2} ohm^{-1} cm.$^{-1}$) "Minimum"	Composition of minimum conductance (moles of H_2O kg.$_{soln.}^{-1}$)
9·66°	0·5700 ± 0·001	0·5685 ± 0·001	0·0023 ± 0·001
25·00	1·0439 ± 0·0005	1·0432 ± 0·0005	0·0019 ± 0·0005
40·00	1·711 ± 0·001	1·710 ± 0·001	0·0015 ± 0·001

DISCUSSION

The Specific Conductances of 100% *and Minimum-conductivity Sulphuric Acid.*—There have been a large number of determinations of either the conductivity of 100% H_2SO_4 or the minimum conductivity of the H_2O–SO_3 system,[7,11-26] The apparatus and techniques

[11] Gillespie and Wasif, *J.*, 1953, 221.
[12] Walden, *Z. anorg. Chem.*, 1902, **29**, 371.
[13] Hantzsch, *Z. phys. Chem.*, 1907, **61**, 257.
[14] Lichty, *J. Phys. Chem.*, 1907, **11**, 225; *J. Amer. Chem. Soc.*, 1908, **30**, 1834.
[15] Bergius, *Z. phys. Chem.*, 1910, **72**, 338.
[16] Poma, *J. Chim. phys.*, 1912, **10**, 187.
[17] Kendall, Adler, and Davidson, *J. Amer. Chem. Soc.*, 1921, **43**, 1846.
[18] Hall and Voge, *J. Amer. Chem. Soc.*, 1933, **55**, 237.
[19] Ussanowitsch, Samarakowa, and Udwenko, *Acta Physicochim. U.R.S.S.*, 1939, **11**, 505; *J. Gen. Chem.* (*U.S.S.R.*), 1939, **9**, 1969.

used in earlier investigations were in general too insensitive and inaccurate to detect the very small differences of composition and of specific conductance between the acid of minimum conductivity and acid of composition H_2SO_4. The values obtained by Lichty,[14] Trenner and Taylor,[6] Brun,[21] Tutundzic and Liler,[23] and Hetherington *et al.*,[24] although less accurate, agree reasonably well with our own values.

The value of the minimum conductivity given by Gillespie and Wasif [11] is appreciably lower that that now obtained. There appear to be two main reasons for this. First, a redetermination of the cell constants of the cells used in the earlier work has shown that the original values were in error by almost 0·5%. Secondly, re-examination of the large-scale plots of the results obtained at 25° by Gillespie and Wasif suggests that they were in error in selecting a value of 0·01033 ohm^{-1} cm.$^{-1}$ for the minimum conductivity, even though a value as low as this was obtained in an individual experiment, and that a value of 0·01040 ohm^{-1} cm.$^{-1}$ would have been more consistent with their results. If these two corrections are made, their corrected value of 0·01045 ohm^{-1} cm.$^{-1}$ agrees reasonably well with the present work.

In calculating the uncertainty in our own value of $(1{\cdot}0439 \pm 0{\cdot}0005) \times 10^{-2}$ ohm^{-1} cm.$^{-1}$ for the specific conductance of 100% sulphuric acid, allowance has been made for the probable effect on the conductivity of small amounts of impurities known to be present in the " AnalaR " acid. In some experiments we measured the conductivity of acid that was known to be impure. Thus, one sample of acid which had become contaminated during storage and was slightly brown gave a reproducible minimum conductivity of 0·01034 ohm^{-1} cm.$^{-1}$—nearly 1% lower than the correct value. It is incorrect to assume that the lower the value of the minimum conductivity the purer the acid, not only because of this result but also because it has been shown that non-electrolytes in general cause a decrease in the conductivity of sulphuric acid.[11] For more accurate work it would be necessary further to reduce the amounts of the impurities in the sulphuric acid, in particular, as has been pointed out by Kunzler and Giauque,[2] of the dissolved air which is soluble to the extent of approximately 0·002 wt. %, and probably causes a slight decrease in the conductivity. It may be seen that our results on the composition of minimum conductance are in agreement with, and extend to other temperatures, those of Kunzler and Giauque.[2] Our determination of the specific conductance of " minimum conductivity " and 100% acid at 9·66°, 25°, and 40° provides values of greater accuracy than hitherto available, and shows that there is a very small difference between the values of these two quantities at each of the temperatures investigated. By assuming that Kunzler and Giauque's 100% acid had the same conductivity as ours at the temperature at which we made our measurements, we were able, by using their temperature coefficient, to calculate a value for their cell constant, and hence obtain conductivity values for their other solutions. Our results agree well with the values thus calculated and we have used these additional values to obtain the minimum conductivity at 9·66° more accurately than would have been possible from our results alone.

Conductivities of Solutions of Water and Sulphur Trioxide in Sulphuric Acid.—Earlier work on the conductivities of solutions of water and sulphur trioxide in sulphuric acid has been discussed by Gillespie and Wasif [11] and compared with their own results. Only Lichty's results [14] for water agreed well with their values.

The results obtained by Gillespie and Wasif and the recent work of Hetherington *et al.*[24] are compared with our own results in Fig. 4. The values obtained by Gillespie and Wasif have been corrected to take account of the errors in their cell constants as mentioned above.

[20] Reinhardt, *J. Amer. Chem. Soc.*, 1950, **72**, 3359.
[21] Brun, *Univ. i. Bergen Arbok*, 1952, *Naturvitenskap. Rekke*, 1953, No. 12, 1.
[22] Schwab, Zentelis, and Kassapoglu, *Chem. Ber.*, 1952, **85**, 508.
[23] Tutundzic and Liler, *Bull. Soc. chim., Belgrade*, 1953, **18**, 521.
[24] Hetherington, Hub, Nichols, and Robinson, *J.*, 1955, 3300.
[25] Tartakowskaya, Bondarenko, and Emelyanova, *Acta Physicochim. U.R.S.S.*, 1937, **6**, 609.
[26] Ussanowitsch and Tartakowskaya, *J. Gen. Chem.* (*U.S.S.R.*), 1946, **16**, 1987.

The upper curve *A* in this figure is the mean curve obtained from our results, and the experimental points are due to Gillespie and Wasif and to Hetherington *et al.* This curve is identical with *B* except that it has been shifted vertically by 0·1 ohm^{-1} cm.$^{-1}$ and to the left, *i.e.*, towards the oleum side, by 0·0019 mole kg.$_{soln.}^{-1}$ so that its minimum occurs at the composition H_2SO_4 since in both these previous investigations it was assumed that the minimum conductivity occurs at this composition. It may be seen that there is generally quite good agreement between these experimental points and our mean curve although the scatter of the points is rather greater than in the present work, and the values of Hetherington *et al.* for solutions of water are somewhat lower than our present values.

Values of the specific conductance of solutions of water and disulphuric acid interpolated from our results are given in Tables 1 and 2. It is believed that they are more accurate than any previous values. They provide a very convenient and a very accurate means of determining the composition of dilute solutions of water or sulphur trioxide in sulphuric acid. They have been used in this way in several recent investigations.[27,28]

We thank the London County Council for a Major County Scholarship (to C. S.). We also thank Mr. E. Roberts, who constructed all the conductivity cells, and Mr. R. H. Flowers who made a few of the conductivity measurements.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, November 6th*, 1956.]

[27] Flowers, Gillespie, and Wasif, *J.*, 1956, 607.
[28] Flowers, Gillespie, and Oubridge, *J.*, 1956, 1925.

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340. *Oxidation of Ethanol by Ceric Perchlorate.*

By MICHAEL ARDON.

The oxidation of ethanol by ceric perchlorate proceeds *via* an intermediate complex between one Ce^{4+} ion and one ethanol molecule. This mechanism explains the kinetic data. The existence of the complex was proved independently by spectrophotometry.

THE kinetics and mechanism of oxidation of organic compounds by ceric perchlorate have been studied recently.[1,2] From their kinetic results on the oxidation of *meso*-2 : 3-butanediol (G) by ceric perchlorate, Duke and Bremer [1] suggested as a mechanism the intermediate formation of a complex or several complexes [*e.g.*, $CeG(H_2O)_4^{4+}$, $CeG_2(H_2O)_2^{4+}$] which decompose by unimolecular disproportionation.

As in much other kinetic work in solution, proof of the suggested mechanism was not sought by other than kinetic evidence, *e.g.*, by independently checking the existence and structure of the intermediate complex. This has been done in the present investigation.

The product of the reaction between ceric perchlorate and ethanol was acetaldehyde, the overall reaction being

$$2Ce^{4+} + EtOH \longrightarrow 2Ce^{3+} + Me{\cdot}CHO + 2H^+$$

This reaction could proceed by either termolecular collision or separate consecutive stages : (*a*) reduction of one ceric ion and production of a univalent radical or ion from the ethanol, and (*b*) the (quick) oxidation of the radical (ion) to acetaldehyde by a second ceric ion. This scheme, suggested by Duke and Bremer for *meso*-2 : 3-butanediol, was found to be correct and the first stage (*a*) was investigated in detail. Stage (*b*), not investigated, is outside the scope of this work. Stage (*a*) is preceded by a reversible formation of a complex between Ce^{4+} and ethanol which undergoes first-order decomposition

[1] Duke and Bremer, *J. Amer. Chem. Soc.*, 1951, **73**, 5179.
[2] Hargraves and Sutcliffe, *Trans. Faraday Soc.*, 1955, **51**, 1105.

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into Ce^{3+} and the radical (ion). This decomposition was found to be the rate-determining step and is followed by stage (*b*).

In many oxidations of organic substrates by quadrivalent cerium an intermediate complex can be clearly seen—the yellow colour deepens, becoming red in higher concentrations, and the absorption spectra, whose peak remains in the near ultraviolet, are extended further into the visible region. This phenomenon is especially noticeable with alcohols.

Ethanol reacts with ceric ions to produce a deep red colour;[3,4] this is most intense with ceric perchlorate, less with the nitrate (owing to formation of the nitrato–ceric complexes) and negligible with the sulphate (owing to formation of the very stable sulphato–ceric complexes). Our object was to determine the role of this complex in the first stage of the oxidation.

Kinetic Measurements.—At a constant pH ($[H^+] = 3{\cdot}2$N) and ionic strength, and a large excess of ethanol, the rate of the reaction was of the first order with respect to the total Ce^{IV} concentration: $-d[Ce^{IV}_{total}]/dt = k[Ce^{IV}_{total}]$.

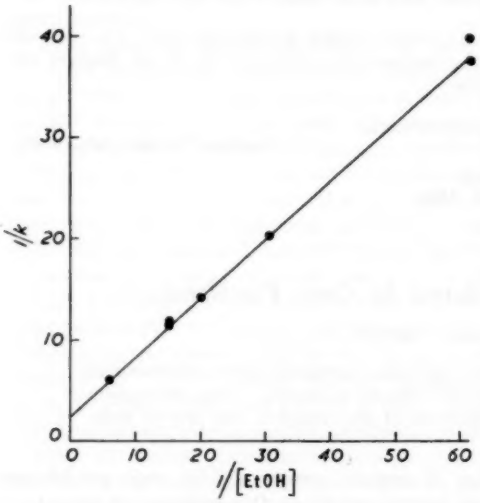


FIG. 1.

The rate was measured either by titration of the remaining Ce^{IV}, or by measuring the optical density of the solution. Both methods gave similar results although the Ce^{IV} concentration was usually 5 times smaller in the spectrophotometric measurements. Since Beer's law is obeyed at a constant and large excess of ethanol, this agreement is to be expected.

The titrimetric method was finally abandoned and only the spectrophotometric method was used, because it allowed the use of lower cerium concentrations; this is desirable because (1) it minimizes the error due to acetaldehyde which is produced during the reaction and can be further oxidized by Ce^{IV} to acetic acid. Towards the end of the reaction this causes a slight increase of the overall rate and therefore a small deviation from the first-order graph. The rate of this side reaction at any fixed point in the main reaction is proportional to the second power of the initial Ce^{IV} concentration and therefore its effect on the overall rate decreases with decrease of the Ce^{IV} concentration; (2) the concentration of dimeric species such as $(Ce{-}O{-}Ce)^{6+}$ is negligible at $[H^+] = 3{\cdot}2$N and the lower concentration of cerium used in the spectrophotometric measurements [5] and thus the only Ce^{IV} species in solution are Ce^{4+} and $CeOH^{3+}$, their ratio being constant at the constant pH and ionic strength which was maintained in the measurement (see p. 1814).

From measurements at different ethanol concentrations it was found that the pseudo-first-order rate constant k obeys the law $1/k = 1/(k'[EtOH]) + 1/k''$. The plot of $1/k$ against $1/[EtOH]$ is a straight line (Fig. 1) which is interpreted as being identical with the well-known graph [1,6] of $1/k = 1/(k_3K[EtOH]) + 1/k_3$.

This relation is derived by assuming the following scheme: Ce^{IV} reacts with ethanol

[3] Meyers and Jacoby, *Z. anorg. Chem.*, 1901, **27**, 359.
[4] Duke and Smith, *Ind. Eng. Chem. Anal.*, 1940, **12**, 201.
[5] Hardwick and Robertson, *Canad. J. Chem.*, 1951, **29**, 818.
[6] Lineweaver and Burk, *J. Amer. Chem. Soc.*, 1934, **56**, 658.

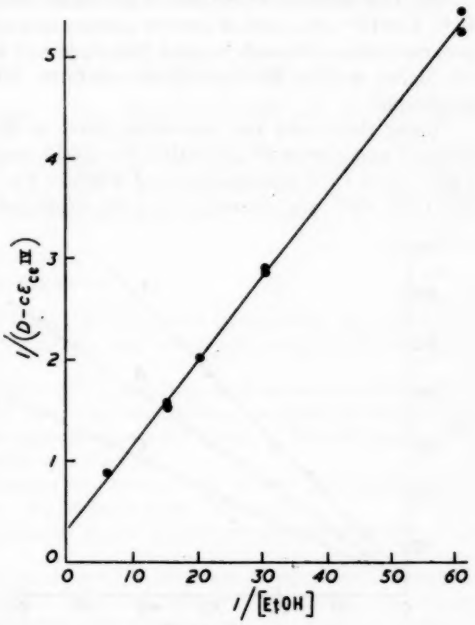
and forms a reversible complex with it, consisting of one ethanol molecule and one ceric ion. The complex decomposes slowly into the products [stage (*a*)]

$$Ce^{IV} + EtOH \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{complex} \xrightarrow{k_3} \text{products}$$

The equilibrium constant of the complex is $k_2/k_1 = K = [\text{complex}]/([Ce^{IV}][EtOH])$; k_3 is the first-order rate constant for the decomposition of the complex and k is the observed rate constant for the disappearance of the total Ce^{IV}. From the graph K was found to be $4{\cdot}3 \pm 0{\cdot}4$ l. mole^{-1} and k_3 $0{\cdot}4 \pm 0{\cdot}04$ min.$^{-1}$.

Fig. 1 shows that the proposed mechanism accords with the kinetic results, but that is insufficient proof of the mechanism because it is not necessarily the only mechanism conforming to them. If one could prove that a complex between ethanol and Ce^{IV} does exist, that its composition is $Ce_1,EtOH_1$ and if, moreover, its equilibrium constant agreed with that calculated from Fig. 1, then the mechanism could be considered proved.

FIG. 2.



Job's method [7] gave an approximate ratio of 1 : 1 for the coloured complex Ce–ethanol but the experimental error was too great, owing to the fact that similar molar concentrations of ethanol and cerium must be used in this method; this caused a too quick decomposition at higher concentrations and a too small difference in light absorption at lower concentrations. Similar difficulties were encountered with other conventional methods. A special method was therefore developed, as follows.

If two species A and B, of which only A is coloured, react, producing a coloured complex (com) AB_n then the optical density D of the solution will be

$$D = c\varepsilon_{com} X + c\varepsilon_A(1 - X) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

ε_A and ε_{com} are the molar extinction coefficient of A and the complex respectively. c is the concentraction of A_{total} and X is the fraction of A combined in the complex. If B is in large excess so that $[B_{total}] \sim [B_{free}]$ and if the only reaction taking place is

$$A + nB \rightleftharpoons AB_n$$

then $$X/\{(1 - X)[B]^n\} = K;\ X = K[B]^n/(1 + K[B]^n) \quad . \quad . \quad . \quad . \quad (2)$$

Insertion of the value of X in (1) gives

$$1/(D - c\varepsilon_A) = 1/\{Kc(\varepsilon_{com} - \varepsilon_A)[B]^n\} - 1/\{c(\varepsilon_{com} - \varepsilon_A)\}$$

Thus the graph representing $1/(D - c\varepsilon_A)$ as a function of $1/[B]^n$ is a straight line if, and only if, the complex has the composition AB_n. In this case one can measure

[7] Job, *Ann. Chim.* (*France*), 1928, **9**, 113; 1936, **6**, 97.

$1/\{c(\varepsilon_{com} - \varepsilon_A)\}$ and $1/K$ from the slope of the graph and its point of intersection with the y axis. This method is practicable only for $n = 1$. Thus the graph of $1/(D - c\varepsilon_A)$ against $1/[B]$ will be a straight line if, and only if, the complex is A_1B_1.* In the experiments at 400 mμ it was found that a straight line is indeed obtained (Fig. 2) and K was found to be $4{\cdot}3 \pm 0{\cdot}7$ l. mole^{-1}, in excellent agreement with the value based on the kinetic data ($4{\cdot}3 \pm 0{\cdot}4$).

Thus the suggested mechanism is considered to be proved.

pH *Dependence.*—Ceric ions in perchloric acid solution consist of the monomeric species Ce^{4+}, $CeOH^{3+}$, etc., and of dimeric species such as $(Ce{-}O{-}Ce)^{6+}$. In low acidity (pH > 0·8) polymerisation proceeds beyond this stage and irreversible colloidal polymers are formed.[8] At higher acidity the hydrolysis constants derived by Hardwick and Robertson [5] are applicable.

Using their data and converting them to 20° we obtained $[CeOH^{3+}][H^+]/[Ce^{4+}] = 3{\cdot}4$ mole l.$^{-1}$ and $[Ce{\cdot}O{\cdot}Ce^{6+}]/[CeOH^{3+}]^2 = 24{\cdot}5$ l. mole^{-1}. At $[H^+] = 3{\cdot}2$N, $[CeOH^{3+}][/Ce^{4+}] = 1{\cdot}06$. At a Ce^{IV} concentration of 0·0035N the dimer $(Ce{-}O{-}Ce)^{6+}$ is only about 2% of the total Ce^{IV} and therefore can be neglected in approximate calculations. The only

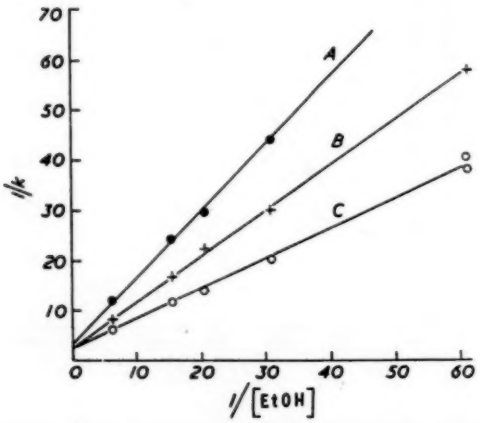


FIG. 3. $[H^+] = A$, 0·79N; B, 1·73N; C, 3·20N.

species existing in quantity are Ce^{4+} and $CeOH^{3+}$ and therefore $[Ce^{4+}]/[Ce^{IV}] = 0{\cdot}49$ where $[Ce^{IV}]$ is the free quadrivalent cerium (not combined with ethanol).

If the complex is between Ce^{4+} and ethanol then K cannot be a real equilibrium constant, but should vary with the pH. By inserting the value of $[Ce^{4+}]$, from the last equation, we can find the real equilibrium constant $\overline{K}$ which is $\overline{K} = [com]/([Ce^{4+}][EtOH]) = 8{\cdot}8 \pm 0{\cdot}8$ l. mole^{-1}. Although K is expected to decrease with decreasing H^+ concentration $\overline{K}$ should remain constant.

In two series of experiments (Fig. 3), K was found to decrease as expected (within experimental error).

$[H^+]$	$K_{calc.}$	K_{found}	$\overline{K}_{calc.}$	$\overline{K}_{found}$
3·2	—	$4{\cdot}3 \pm 0{\cdot}4$	8·8	—
1·73	$2{\cdot}9 \pm 0{\cdot}3$	$2{\cdot}7 \pm 0{\cdot}4$	8·8	$8{\cdot}1 \pm 1{\cdot}1$
0·79	$1{\cdot}7 \pm 0{\cdot}2$	$1{\cdot}8 \pm 0{\cdot}4$	8·8	$9{\cdot}5 \pm 2$

The pH dependence confirms the assumption that only Ce^{4+} and not its hydrolysis products take part in the complex formation. The assumption is further supported by

* This method was used by Benesi and Hildebrand [9] for the special case where $\varepsilon_A = 0$.

[8] Ardon and Stein, *J.*, 1956, 104.

[9] Benesi and Hildebrand, *J. Amer. Chem. Soc.*, 1949, **71**, 2703.

the fact that the value of k_3 is the same at different H^+ concentrations. This proves that there is only one (and the same) complex which decomposes, as described. It should be remembered that in these experiments the ionic strength was not kept constant and therefore a slight deviation from the calculated value is expected, but this does not exceed the experimental error. On the other hand, an attempt to keep the ionic strength constant by substituting Na^+ for H^+ causes a very large positive deviation because Na^+ is much more hydrated [10] than H^+ and at a concentration of 3N in Na^+ it causes a drastic decrease in the activity of water. The concentration of water enters the equilibrium constant because the reaction is in fact

$$Ce(H_2O)_6^{4+} + EtOH \rightleftharpoons Ce(H_2O)_5,EtOH^{4+} + H_2O$$

and therefore a much higher concentration of the complex at high salt concentrations is expected.

Higher complexes such as $Ce(EtOH)_2^{4+}$, $Ce(EtOH)_3^{4+}$, etc., are very likely to exist in higher ethanol concentrations than those used here, but the results point to the fact that no appreciable amounts are formed with the ethanol concentrations used.

Experimental

Ceric Perchlorate Solution.—Ceric hydroxide, $Ce(OH)_4$, was precipitated by ammonium hydroxide from a solution of ceric ammonium nitrate, and rinsed with water until all trace of ammonia was removed.

The hydroxide was reduced by hydrogen peroxide in perchloric acid and an acidified solution of cerous perchlorate resulted from which ceric perchlorate was prepared by electrolytic oxidation; the resulting solution was 0·366M in total cerium and 0·358—0·350N in quadrivalent cerium. The concentration of perchloric acid was 3·2N.

Ethanol was redistilled and its concentration was found to be 16·55M (from the density). Triply distilled water was used throughout. All reagents were " AnalaR."

Acetaldehyde was determined gravimetrically as the 2 : 4-dinitrophenylhydrazone. The yield was 90%.

Spectrophotometric measurements were made with a Beckman B Spectrophotometer at 400 mμ. A two compartment cell (similar to a Thunberg tube) was constructed by addition of a side compartment to a 1 cm. Beckman Pyrex cell, which permits the separate storage of two liquids which can be mixed by inverting the cell.

1 ml. of the ceric solution (diluted 1 : 10 with 3·2N-perchloric acid) was placed in one compartment, and a measured amount of diluted ethanol in the other. Enough 4·7N-perchloric acid and water were added to make the final concentration of perchloric acid 3·2N and the final volume 10 ml.

After being kept for 20 min. in a thermostat at 20° ± 0·05° the liquids were mixed and at specific intervals (1—10 min.) the cell was removed and dried and the optical density was measured. The measurement took about 10 sec. and the temperature variation due to removal from the thermostat did not exceed 0·1°.

The measurements for determination of the complex structure were made in the same way, but the cell was dried before mixing; in this way the time of measurement was reduced to 6 sec. The small error (less than 2%) due to decomposition during these 6 sec. was calculated from the known value of the rates of decomposition, and the results were adjusted accordingly.

I thank Professor G. Stein of this University for helpful suggestions and discussion.

Department of Physical Chemistry,
Hebrew University, Jerusalem, Israel. [*Received, November 13th*, 1956.]

[10] Cf. International Critical Tables, Vol. 6, p. 311; Glasstone, " Textbook of Physical Chemistry," Macmillan, London, 1951, p. 921.

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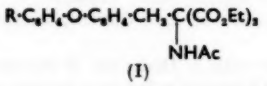
341. *Cyto-active Amino-acids and Peptides. Part III.*[1,2] *Synthesis of* para-*Substituted Phenyl and Alkoxymethyl Ethers of Tyrosine.*

By F. Bergel and G. E. Lewis.

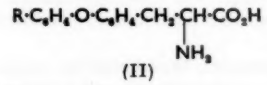
O-[*p*-Di-(2-chloroethyl)aminophenyl]-DL-tyrosine has been synthesised by two routes. Etherification of *N*-acyl-L-tyrosine esters with *p*-fluoronitrobenzene led to racemisation. Attempts to resolve *N*-acetyl-*O*-*p*-nitrophenyl-DL-tyrosine failed. Methoxymethyl and ethoxymethyl ethers of L-tyrosine have been prepared.

In Parts I [1] and II [2] of this series the preparation of novel *para*-substituted phenylalanines was described. One of them, *p*-di-(2-chloroethyl)amino-L-phenylalanine (CB 3025) was found to be very active against an experimental animal tumour,[3] to cause mutations in *Drosophila melanogaster*,[4] chromosome damage in tumour cells,[5] and inhibition of phenylalanine uptake in *Staph. aureus*.[6] In continuation of this work, syntheses of *para*-substituted phenyl and alkoxymethyl ethers of tyrosine were undertaken as a step towards the study of corresponding iodinated derivatives.

O-[*p*-Di-(2-chloroethyl)aminophenyl]-DL-tyrosine [II; R = $(Cl\cdot CH_2\cdot CH_2)_2N$] was obtained from diethyl acetamido-*p*-(*p'*-nitrophenoxy)benzylmalonate [7] (I; R = NO_2) *via* the *p'*-amino-compound [7] (I; R = NH_2), the preparative sequence being continued with hydroxyethylation, chlorination, and hydrolysis, in a manner published previously.[1] The reduction stage was improved and the di-(2-hydroxyethyl)amino-intermediate [I; R = $(HO\cdot CH_2\cdot CH_2)_2N$] was obtained crystalline. However, no attempt was made to isolate the malonate [I; R = $(Cl\cdot CH_2\cdot CH_2)_2N$], the chlorination product from the dialcohol [I; R = $(HO\cdot CH_2\cdot CH_2)_2N$] being hydrolysed directly to the required amino-acid [II; R = $(Cl\cdot CH_2\cdot CH_2)_2N$].



(I)



(II)

Attempts to synthesise the optically active forms of the tyrosine [II; R = $(Cl\cdot CH_2\cdot CH_2)_2N$], in particular the L-isomer, in view of the biological results in the phenylalanine series,[3] failed in every instance when *p*-fluoronitrobenzene was used with a number of *N*-acyl-L-tyrosine esters. Although etherification was achieved in reasonable yields, in presence of anhydrous potassium carbonate in ethyl methyl ketone, it was always accompanied by racemisation of the tyrosine ethers produced. In consequence, only the DL-forms of *N*-formyl-, *N*-benzoyl-, and *N*-phthaloyl-*O*-(*p*-nitrophenyl)tyrosine ethyl esters were obtained. That this was due to the vigorous conditions necessary to effect etherification was shown by the results with fluoro-2 : 4-dinitrobenzene which, when condensed with *N*-formyl-L-tyrosine ethyl esters under milder conditions, gave the (2 : 4-dinitrophenyl)-*N*-formyl-*O*-L-tyrosine ester. We also confirmed the claim by Canzanelli *et al.*[8] that 3 : 4 : 5-tri-iodo-1-nitrobenzene, condensed with *N*-benzoyl-L-tyrosine ethyl ester, yields the L-form of di-iodinated *O*-*p*-nitrophenyltyrosine. *N*-Formyl-*O*-(*p*-nitrophenyl)-DL-tyrosine ethyl ester was reduced to the amino-compound, hydroxyethylated, chlorinated, and hydrolysed to the "mustard" derivative [II; R = $(Cl\cdot CH_2\cdot CH_2)_2N$], identical with

[1] Part I, Bergel and Stock, *J.*, 1954, 2409.
[2] Part II, Bergel, Burnop, and Stock, *J.*, 1955, 1223.
[3] Bergel, Haddow, and Stock, *B.E.C.C. Ann. Report*, 1953, **31**, 6.
[4] Fahmy and Fahmy, *J. Genet.*, 1956, **54**, 146.
[5] Koller and Veronesi, *Brit. J. Cancer*, in the press.
[6] Crathorn and Hunter, *Biochem. J.*, in the press.
[7] Southwick, Foltz, and McIntyre, *J. Amer. Chem. Soc.*, 1953, **75**, 5877.
[8] Canzanelli, Harington, and Randall, *Biochem. J.*, 1934, **28**, 68.

the product from the malonic ester synthesis reported above. In the case of the *O*-*p*-nitrophenyl-*N*-phthaloyltyrosine ethyl ester, reduction gave the corresponding amine which, like its precursor, showed no optical activity.

Our next efforts were towards the resolution of *N*-acetyl-*O*-*p*-nitrophenyl-DL-tyrosine by formation of salts with optically active bases such as brucine, quinine, cinchonine, cinchonidine, strychnine, and (+)-amphetamine. In no case were satisfactory results obtained. Equally unsuccessful was the application of the enzyme acylase I to the same tyrosine derivative under conditions similar to those used by Greenstein *et al.*[9] in the resolution of *N*-acetyl-DL-*alloiso*leucine.

In addition to the above phenyl ethers we prepared alkoxymethyl ethers of tyrosine, starting with *N*-phthaloyl-L-tyrosine ethyl ester. When this compound was allowed to react with chloromethyl methyl or ethyl ether and the phthaloyl group was removed with ethanolic hydrazine, *O*-methoxymethyl- and *O*-ethoxymethyl-L-tyrosine were obtained. Both products, in contrast to tyrosine, were easily soluble in water and liberated formaldehyde in warm dilute mineral acids. It was thought possible that this characteristic would enable these compounds to release formaldehyde slowly under biological conditions and that they would act as anti-tumour agents. However, no such effect was achieved with *O*-methoxymethyl-L-tyrosine (CB 3081) when applied by A. Haddow [10] to rats carrying the implanted Walker carcinoma 256.

Negative biological results were also obtained with the compound [II; R = $(Cl{\cdot}CH_2{\cdot}CH_2)_2N$] (CB 3051). This is surprising in view of the high activity of the *p*-di-(2-chloroethyl)aminophenylalanine.[3] On the other hand, Fahmy and Fahmy [11] observed point mutations with CB 3051 in *Drosophila melanogaster*.

Experimental

O-[p-*Di*-(2-*chloroethyl*)*aminophenyl*]-DL-*tyrosine* [II; R = $(Cl{\cdot}CH_2{\cdot}CH_2)_2N$].—*Method* (1). (*a*) The nitro-compound (I; R = NO_2), prepared as described by Southwick *et al.*,[7] had m. p. 154° (lit., 153·5—154°); it (8·88 g.) was hydrogenated in ethyl acetate (200 ml.) and methanol (50 ml.) at atmospheric pressure in presence of palladised calcium carbonate (0·5 g.). After filtration, the solvent was evaporated *in vacuo* and the residue dissolved in warm benzene (charcoal), which was filtered again. The cool solution on admixture with a small amount of light petroleum yielded, almost quantitatively, colourless crystals of the amine (I; R = NH_2) which, recrystallised from ethanol–light petroleum, had m. p. 150° (lit., m. p. 147—148°).

(*b*) Ethylene oxide (12 ml.) was added to a solution of the amino-compound (I; R = NH_2) (5·0 g.) in water (75 ml.) and glacial acetic acid (45 ml.). The mixture was kept at 20° for 24 hr., then neutralised by solid sodium hydrogen carbonate. The precipitated gum was extracted with ethyl acetate, and the solution dried (Na_2SO_4), treated with charcoal, and, after filtration, evaporated *in vacuo* to dryness. The residue (yield 65%), crystallised from benzene–light petroleum, gave the required *di*(*hydroxyethyl*)*amino-compound* [I; R = $(HO{\cdot}CH_2{\cdot}CH_2)_2N$] as colourless needles, m. p. 104—105° (Found: C, 62·3; H, 7·1; N, 5·7. $C_{26}H_{34}O_8N_2$ requires C, 62·2; H, 6·8; N, 5·6%).

(*c*) The foregoing compound (5 g.) was dissolved in sodium-dried benzene (200 ml.) and *ca.* 50 ml. of the solvent were distilled off, in order to remove any traces of water. To the cooled solution was added phosphorus oxychloride (15 ml.), and the whole then heated under reflux for 25 min. The benzene was removed *in vacuo*, and the residue dissolved in concentrated hydrochloric acid (120 ml.), refluxed for 6 hr., and concentrated to a thick syrup *in vacuo*. This was dissolved in water (40 ml.), and the solution treated with charcoal, filtered, and neutralised by saturated sodium acetate solution, whereupon the O-[p-*di*-(2-*chloroethyl*)*aminophenyl*]-DL-*tyrosine* was deposited as a heavy off-white precipitate (35%). Recrystallised from aqueous methanol, it had m. p. 159—160° (decomp.) (Found: C, 57·2; H, 5·9; N, 7·0; Cl, 18·2. $C_{19}H_{22}O_3N_2Cl_2$ requires C, 57·4; H, 5·6; N, 7·1; Cl, 17·8%).

Method (2). (*a*) *N*-Formyltyrosine ethyl ester was mentioned by Haas *et al.*[12] but no details

[9] Greenstein, Birnbaum, and Levintow, *Biochem. Preparations*, 1953, **3**, 87.
[10] Haddow, personal communication.
[11] Fahmy and Fahmy, personal communication.
[12] Haas, Sizer, and Loofbourow, *Biochim. Biophys. Acta*, 1951, **6**, 1589.

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were given. In the present investigation it was prepared by treating L-tyrosine ethyl ester (5 g.) with 98% formic acid (25 ml.) and acetic anhydride (4 ml.) at 40—50° for ¾ hr. The solvent was removed *in vacuo* and the residue diluted with water (250 ml.). The aqueous solution was saturated with sodium chloride and extracted with ethyl acetate. The extract was dried (Na_2SO_4) and concentrated to a small volume. Addition of ether precipitated *N*-formyl-L-tyrosine ethyl ester (75%), m. p. 105—106° (lit., 105—106°), $[\alpha]_D^{23}$ +37·2° (*c* 4·65 in EtOH) (Found: C, 60·5; H, 6·4; N, 5·9. Calc. for $C_{12}H_{15}O_4N$: C, 60·8; H, 6·4; N, 5·9%).

(*b*) This material (11·8 g.) and *p*-fluoronitrobenzene (7·0 g.) in freshly dried, redistilled ethyl methyl ketone (200 ml.) were refluxed for 48 hr. over finely powdered anhydrous potassium carbonate (3·5 g.), and the solution was filtered, and taken to dryness *in vacuo*. The residue was dissolved in ethyl acetate, and the solution washed with water, dried (Na_2SO_4), and evaporated to a small volume. After dilution with ether, addition of a small amount of pentane and storage in the refrigerator overnight, gave colourless N$^{\alpha}$-*formyl*-O-p-*nitrophenyl*-DL-*tyrosine ethyl ester* (40%), m. p. 105°, α 0° (Found: C, 60·4; H, 5·4; N, 7·8. $C_{18}H_{18}O_6N_2$ requires C, 60·3; H, 5·4; N, 7·8%).

(*c*) The nitro-compound (4·78 g.) in ethyl acetate (100 ml.) and methanol (25 ml.) was hydrogenated in the presence of palladised calcium carbonate (0·2 g.). The filtered solution was washed with water, dried (Na_2SO_4), and taken to dryness. N$^{\alpha}$-Formyl-*O*-*p*-aminophenyl-DL-tyrosine ethyl ester was left as oil (yield 70%).

It gave an *acetyl derivative* which crystallised from aqueous ethanol as a monohydrate, m. p. 85·5° (Found: C, 61·8; H, 6·3; N, 7·1. $C_{20}H_{22}O_5N_2,H_2O$ requires C, 61·8; H, 6·2; N, 7·2%). The amine and its acetyl derivative were optically inactive.

(*d*) The amine was hydroxyethylated and chlorinated as for the malonic ester intermediate. After acid hydrolysis the *O*-[*p*-di-(2-chloroethyl)aminophenyl]-DL-tyrosine was obtained, identical in m. p. and mixed m. p. with the product obtained by method (1).

O-p-*Nitrophenyl*-N-*phthaloyl*-DL-*tyrosine Ethyl Ester*.—(*a*) Equivalent amounts of L-tyrosine ethyl ester and phthalic anhydride were dissolved in benzene, the solvent was removed, and the reactants were heated as a thick oil on the water-bath for 30 min. The product was refluxed in 2·5N-ethanolic hydrogen chloride for 1½ hr., then evaporated to dryness *in vacuo*, and ethyl acetate added to the residual oil. While the phthaloyl compound was dissolved by the ethyl acetate, unchanged amino-ester was deposited as the solid hydrochloride. The ethyl acetate solution was filtered, washed with aqueous sodium carbonate, and, after drying (Na_2SO_4), concentrated to a small volume. Addition of pentane precipitated oily N-*phthaloyl*-L-*tyrosine ethyl ester* which solidified (yield 75%). A small portion was recrystallised from *cyclo*hexane, giving white needles, m. p. 104—105°, $[\alpha]_D^{20}$ −192° (*c* 2·01 in EtOH) (Found: C, 67·1; H, 5·2; N, 4·2. $C_{19}H_{17}O_5N$ requires C, 67·3; H, 5·1; N, 4·1%).

(*b*) This material was etherified by *p*-fluoronitrobenzene under the conditions used for the *N*-formyl compound. After evaporation of the filtered ketonic solution, an oil (*ca.* 60%) was obtained which crystallised readily upon addition of ethanol. Recrystallisation from ethanol gave O-p-*nitrophenyl*-N-*phthaloyl*-DL-*tyrosine ethyl ester* as colourless prisms, m. p. 116°, α 0° (Found: C, 65·1; H, 4·4; N, 6·1. $C_{25}H_{20}O_7N_2$ requires C, 65·2; H, 4·4; N, 6·1%).

O-p-*Aminophenyl*-N$^{\alpha}$-*phthaloyl*-DL-*tyrosine Ethyl Ester*.—The nitro-compound (15 g.) in ethyl acetate (200 ml.) and methanol (50 ml.) was hydrogenated over palladised calcium carbonate (0·5 g.). The filtered solution was shaken with water to remove methanol, separated, dried (Na_2SO_4), and taken to dryness. The residual oil crystallised overnight (yield 80%). It recrystallised from propan-2-ol as light yellow needles, m. p. 121—122°, α 0° (Found: C, 70·2; H, 5·1; N, 6·6. $C_{25}H_{22}O_5N_2$ requires C, 69·8; H, 5·2; N, 6·5%).

N-*Benzoyl*-O-p-*nitrophenyl*-DL-*tyrosine Ethyl Ester*.—*N*-Benzoyl-L-tyrosine ethyl ester was prepared according to Canzanelli *et al.*;[8] it had m. p. 122—123°, $[\alpha]_D^{20}$ −15·3° (*c* 3·0 in ethyl methyl ketone), $[\alpha]_D^{20}$ −23·7° (*c* 3·7 in EtOH). It was treated with *p*-fluoronitrobenzene as above. The oil obtained after filtration and evaporation of the ketone crystallised in *ca.* 60% yield on addition of ethanol. Recrystallisation from the same solvent gave colourless needles, m. p. 145—146°, α 0° (Found: C, 66·5; H, 5·2; N, 6·1. $C_{24}H_{22}O_6N_2$ requires C, 66·4; H, 5·1; N, 6·5%).

N$^{\alpha}$-*Formyl*-O-(2 : 4-*dinitrophenyl*)-L-*tyrosine Ethyl Ester*.—*N*-Formyl-L-tyrosine ethyl ester in an exact equivalent of aqueous N-sodium hydroxide was heated with an equivalent amount of 1-fluoro-2 : 4-dinitrobenzene in ethanol on the water-bath for 30 min.; water was added to precipitate the *dinitrophenyl tyrosine ether* (75%). The product solidified and, recrystallised

from benzene–pentane, had m. p. 92—93°, $[\alpha]_D^{18}$ +18° (*c* 1·8 in EtOH) (Found : C, 53·4; H, 4·3; N, 10·6. $C_{16}H_{17}O_6N_3$ requires C, 53·6; H, 4·3; N, 10·4%).

Attempts to Resolve N-*Acetyl*-O-p-*nitrophenyl*-DL-*tyrosine*.—This compound, prepared by the method of Southwick *et al.*,[7] had m. p. 162°. (*a*) It was mixed with equimolecular proportions of brucine, cinchonine, cinchonidine, quinine, strychnine, or (+)-amphetamine in ethanol; *e.g.*, brucine (3·94 g.) in ethanol (10 ml.) was mixed with the tyrosine derivative (3·44 g.) in ethanol (15 ml.). No crystals were deposited during several days' storage at 20°. Evaporation gave a gum. When strychnine (3·34 g.) was used, the insolubility of the base required larger amounts of ethanol (75 ml.). In no case, including the use of methanol, chloroform, or aqueous ethanol (70%) as solvents, were satisfactory results obtained.

(*b*) The tyrosine derivative was treated in the manner described by Greenstein *et al.*[9] for acetyl-DL-*alloiso*leucine, in an aqueous solution of lithium hydroxide with dry acylase I powder. No preferential enzymic hydrolysis was observed.

O-*Methoxymethyl*-L-*tyrosine*.—*N*-Phthaloyl-L-tyrosine ethyl ester (10 g.) and an excess of chloromethyl methyl ether (25 ml.) in dry benzene (200 ml.) were refluxed over dry potassium carbonate (5 g.) for 13 hr. The solution was filtered and evaporated *in vacuo*. The residual gum was extracted with a very large volume of boiling light petroleum (b. p. 60—80°) from which slowly crystallised, on cooling, O-*methoxymethyl*-N-*phthaloyl*-L-*tyrosine ethyl ester* (75%) as colourless needles, m. p. 75—76°, $[\alpha]_D^{20}$ −191° (*c* 3·01 in C_6H_6) (Found : C, 65·7; H, 5·75; N, 3·9. $C_{21}H_{21}O_6N$ requires C, 65·8; H, 5·5; N, 3·7%).

This compound was refluxed in an equivalent of M-ethanolic hydrazine for 2 hr., then cooled and filtered to remove phthalhydrazide, and the filtrate evaporated to dryness. The residue was passed in benzene down a column of alumina to remove any traces of phthalhydrazide. The eluate on evaporation gave an oil which was hydrolysed to the amino-acid by shaking it with a slight excess of N-sodium hydroxide at 20° for 2—3 hr. Most of the oil dissolved in the alkaline solution, which was then filtered and neutralised with an exact equivalent of N-acetic acid. The solution was then evaporated *in vacuo* at 40—50° until solid material was deposited. A large excess of ethanol was then added to precipitate completely the O-*methoxymethyl*-L-*tyrosine* (yield 40%). Recrystallised from aqueous ethanol, it had m. p. 185—190° (decomp.) on slow heating, $[\alpha]_D^{23}$ −27·5° (*c* 2·00 in H_2O) (Found : C, 58·5; H, 6·9; N, 6·2. $C_{11}H_{15}O_4N$ requires C, 58·65; H, 6·7; N, 6·2%).

On warming a solution of the compound (0·25 g.) in N-hydrochloric acid (5 ml.) in a stoppered tube for 1—2 min., an odour of formaldehyde was produced. Neutralisation with N-sodium hydroxide precipitated L-tyrosine. The filtrate on addition of ethanolic dimedone deposited the formaldehyde derivative (m. p. and mixed m. p.).

O-*Ethoxymethyl*-L-*tyrosine*.—In the same manner chloromethyl ethyl ether and *N*-phthaloyl-L-tyrosine ethyl ester gave O-*ethoxymethyl*-L-*tyrosine* (*ca.* 10%) without crystallisation of the intermediate *N*-phthaloyl ethyl ester. The compound, recrystallised from aqueous ethanol, had m. p. 188—190° (decomp.), $[\alpha]_D^{21}$ −20·5° (*c*, 1·00 in H_2O) (Found : C, 59·8; H, 7·0; N, 6·0. $C_{12}H_{17}O_4N$ requires C, 60·2; H, 7·2; N, 5·9%).

We thank Dr. J. P. Greenstein of the National Cancer Institute, National Institutes of Health, Bethesda, U.S.A., for a gift of acylase I, and all our biological colleagues, particularly Professor A. Haddow, for their interest and co-operation. One of us (G. E. L.) acknowledges the grant of a Junior Fellowship of the British Empire Cancer Campaign. This work has been supported by grants to this Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

CHESTER BEATTY RESEARCH INSTITUTE,
INSTITUTE OF CANCER RESEARCH : ROYAL CANCER HOSPITAL,
FULHAM ROAD, S.W.3.

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342. *Studies in the Chemistry of Quadrivalent Germanium. Part IV.* The Chemical Nature of Solutions of Quadrivalent Germanium in Hydrochloric or Hydrobromic Acid.*

By D. A. Everest and J. C. Harrison.

Solubility measurements and anion-exchange studies have indicated that anionic germanium chloro-complexes of the type $[Ge(OH)_xCl_{6-x}]^-$ or $[Ge(OH)_xCl_{6-x}]^{2-}$, where x lies between 3 and 4, are the principle germanium species present in 6—9M-hydrochloric acid solutions. Below 6M-hydrochloric acid, these complexes are hydrolysed to germanium dioxide, and above 9M-hydrochloric acid they are converted into germanium tetrachloride. No evidence has been found for the existence of any germanium bromo-complexes in hydrobromic acid solution.

Little information exists as to the chemical nature of solutions of germanium tetrachloride in hydrochloric acid of sufficient strength to prevent hydrolysis to germanium dioxide (*i.e.*, >6M). Allison and Muller [1] showed that the solubility of germanium tetrachloride increased from a low value in 12M-hydrochloric acid to a maximum value in 7·8M-acid. Pugh [2] showed that the solubility of germanium dioxide was a minimum in 6N-hydrochloric acid, but that its solubility increased at higher acid concentrations. No quantitative experiments were made by these authors at acid concentrations between 6 and 7·8M. Transport experiments [3] failed to establish the presence of anionic germanium complexes in hydrochloric acid solutions, although it was possible to isolate cæsium hexachlorogermanate under the correct conditions.

Adsorption of germanium on a large excess of anion-exchange resin from very dilute solutions of quadrivalent germanium in hydrochloric acid has been reported by Yoshino [4] and by Nelson and Kraus.[5] This work gave little information, however, concerning the complexes which occur in more concentrated germanium solutions. In the present work, ion-exchange experiments have been carried out with solutions of quadrivalent germanium in hydrochloric acid, under conditions which allowed sufficient germanium to be sorbed by the resin to enable the formulæ of the sorbed germanium complexes to be calculated by the usual methods (cf., *e.g.*, Salmon [6]).

Experimental

Solubility Measurements.—The solubilities of germanium dioxide tetrachloride and bromide in hydrochloric and hydrobromic acid were determined by shaking excess of the germanium compound with the required acid at room temperature for 2—3 weeks, and then analysing the solution phase for germanium. The solutions obtained in this way were used in the equilibrium experiments with the anion-exchangers.

Anion-exchangers.—Analytical Grade Amberlite I.R.A. 400, in the chloride or bromide form, was used throughout; 0·25 g. of the air-dried chloride form of the batch of resin used had a capacity of *ca.* 0·73 milliequiv.

Analytical Methods.—Germanium was determined iodometrically after reduction to the bivalent state.[7] Halogens were determined gravimetrically as the silver halide. Rubidium was determined by first volatilising germanium by fuming with 12M-hydrochloric acid, fuming with sulphuric acid, and igniting to rubidium sulphate.

Anion-exchange Experiments.—Continuous shaking for 24 hr. was allowed for establishment

* Part III, *J.*, 1955, 4415.

[1] Allison and Muller, *J. Amer. Chem. Soc.*, 1932, **54**, 2833.
[2] Pugh, *J.*, 1929, 1537.
[3] Laubengayer, Billings, and Newkirk, *J. Amer. Chem. Soc.*, 1940, **62**, 546.
[4] Yoshino, *Bull. Chem. Soc. Japan*, 1955, **28**, 382.
[5] Nelson and Kraus, *J. Amer. Chem. Soc.*, 1955, **77**, 2133.
[6] Salmon, *Rev. Pure Appl. Chem.* (*Australia*), 1956, **6**, 24.
[7] Everest, *J.*, 1953, 4117.

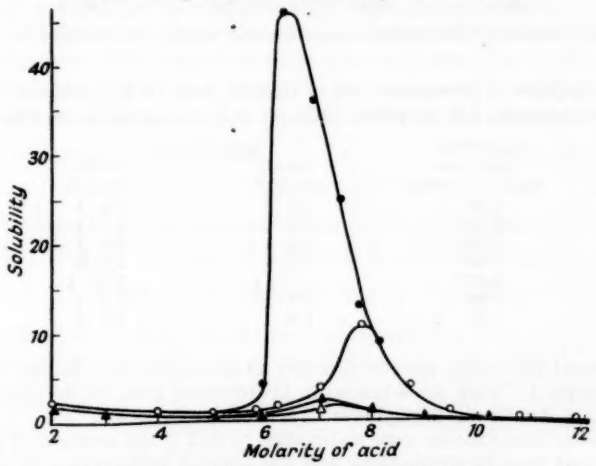
of equilibrium between the resin and the solution phase, experiments for longer periods showing this to be sufficient. The bulk of the solution was then decanted from the resin, and the latter transferred to a column (1 cm. int. diam., 10 cm. long above the sintered disc of No. 2 grade porosity) with the minimum amount of hydrochloric acid of the same normality as in the original solution. The acid adhering to the outside of the resin particles was removed by flushing the column for 2—3 sec. with water under high suction. The resin was then eluted with 0·1M-sodium hydroxide (250 ml.) for 24 hr. to remove germanium and chloride, which were then determined in the eluate. Blank experiments with 6—8M-hydrochloric acid and 0·25 g. of resin showed that a value of 0·05 milliequiv. had to be subtracted from the value of the chloride sorbed by the resin in order to correct for the free acid present in the resin phase.

Rubidium Hexachlorogermanate.—To a saturated solution of germanium tetrachloride in 7M-hydrochloric acid (15 ml.) was added a solution of rubidium chloride (1·5 g.) in 7M-hydrochloric acid (5 ml.); on cooling, crystals of the *salt* separated (Found: Rb, 37·0; Ge, 15·6; Cl, 46·8. Rb_2GeCl_6 requires Rb, 37·4; Ge, 15·9; Cl, 46·6%). Cæsium hexachlorogermanate was prepared by an analogous reaction.

Results

Solubility Measurements.—The solubilities of germanium dioxide and tetrachloride in hydrochloric acid are shown in the Figure. The salient feature is the large divergence between the

Solubilities of germanium tetrachloride and germanium dioxide in hydrochloric acid and of germanium tetrabromide and germanium dioxide in hydrobromic acid.



● Germanium tetrachloride in hydrochloric acid.
○ Germanium dioxide in hydrochloric acid.
▲ Germanium tetrabromide in hydrobromide acid.
△ Germanium dioxide in hydrobromic acid.

(Solubilities expressed in grams of germanium dioxide per litre.)

solubility curves for germanium dioxide and tetrachloride at hydrochloric acid concentrations between 6 and 8M, indicating that the simple equilibrium $GeO_2 + 4HCl \rightleftarrows GeCl_4 + 2H_2O$ does not hold in this acid concentration range. The corresponding divergence, and the actual germanium solubilities, are much smaller in the hydrobromic acid solutions. All solutions of germanium tetrachloride in hydrochloric acid are stable above 7M-hydrochloric acid with respect to hydrolysis, no precipitate of germanium dioxide occurring even after one year. Similar solutions in 6M-hydrochloric acid, or below, begin to afford precipitates of germanium dioxide after a few hours and may continue to do this for several weeks. Solutions in 6·5M-hydrochloric acid are stable for some 4—5 months but then begin to slowly deposit germanium dioxide. The solubility of germanium tetrachloride in 6—8M-hydrochloric acid showed an inverse temperature coefficient of solubility; solubilities found were: 49·3 g./l. of germanium dioxide at −15°, 46·3 at 0°, 38·7 at 15°, and 33·5 at 35°.

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Ion-exchange Experiments.—The sorptions of germanium dioxide and of chloride by Amberlite I.R.A. 400-Cl from hydrochloric acid solutions (6·5—9M) saturated with germanium dioxide or tetrachloride are given in Table 1. Outside this range of hydrochloric acid concentrations the sorption of germanium was too small to be measured by the purely chemical techniques used in this work, owing to the low solubility of the germanium (see Figure); measurable sorption of

TABLE 1. *Sorption of germanium and of chloride from hydrochloric acid solutions by Amberlite* I.R.A. 400-Cl (0·25 *g.*).

HCl concn. (M) *	Cl sorbed (mole per equiv. of resin)	Ge sorbed (mole per equiv. of resin)	Vol. of soln. taken (ml.)	Ratio Cl : Ge in resin phase : singly charged	doubly charged
Germanium tetrachloride in hydrochloric acid					
6·5	1·64	0·67	10	1·9 : 1	2·9 : 1
6·5	1·25	0·595	10	1·4 : 1	2·4 : 1
7·0	1·10	0·42	50	1·2 : 1	2·2 : 1
7·0	1·34	0·485	50	1·7 : 1	2·7 : 1
7·0	1·10	0·39	5	1·3 : 1	2·3 : 1
7·5	1·25	0·39	10	1·65 : 1	2·65 : 1
7·5	1·37	0·395	10	1·9 : 1	2·9 : 1
8·0	1·10	0·15	50	1·65 : 1	2·65 : 1
Germanium dioxide in hydrochloric acid					
8·0	1·06	0·195	50	1·3 : 1	2·3 : 1
9·0	1·05	0·08	50	1·6 : 1	2·6 : 1

* Concentration before addition of germanium dioxide or tetrachloride.

TABLE 2. *Sorption of germanium and of chloride from* 7M*-hydrochloric acid* (10 *ml.*) *by Amberlite* I.R.A. 400-Cl (0·25 *g.*) *and its dependence on time.*

Cl sorbed (mole per equiv. of resin)	Ge sorbed (mole per equiv. of resin)	Ratio Cl : Ge, singly charged	doubly charged	Time of pre-ageing (days)
1·11	0·39	1·3 : 1	2·3 : 1	1
1·17	0·415	1·4 : 1	2·4 : 1	3
1·04	0·355	1·3 : 1	2·3 : 1	9
1·04	0·34	1·3 : 1	2·3 : 1	15
1·07	0·475	1·15 : 1	2·15 : 1	43
1·37	0·46	1·8 : 1	2·8 : 1	70
1·17	0·37	1·5 : 1	2·5 : 1	300

germanium occurred only when the concentration of germanium in solution was greater than *ca.* 30 mg.-atoms per l. With the solutions in hydrobromic acid, the sorption of germanium by Amberlite I.R.A. 400-Br was negligible at all acid concentrations.

In addition some experiments were undertaken to find if the sorption of germanium and chloride by the resin from 7M-hydrochloric acid was affected by pre-ageing of the experimental solutions (Table 2). No appreciable effect was found with pre-ageing periods of 1—300 days.

DISCUSSION

The ratios chloride : germanium in the adsorbed complexes (calculated as previously described [8]) are given in Tables 1 and 2. The low ratios found (cf. 5 : 1 for $GeCl_5^-$ or 6 : 1 for $GeCl_6^{2-}$) indicate that partly hydrolysed species, *i.e.*, $[Ge(OH)_xCl_{5-x}]^-$, or $[Ge(OH)_xCl_{6-x}]^{2-}$, are being adsorbed by the resin, the experimental results appearing to favour values of x between 3 and 4. As the sorption of germanium approaches, and in some cases exceeds, 0·5 mg.-atom per equiv. of resin, it is considered probable that it is the univalent complex which is actually taken up by the resin (cf. ref. 9).

The solubility curves obtained (Figure) show that soluble germanium complexes occur to a marked extent only in 6—9M-hydrochloric acid. It is suggested that an

[8] Everest and Harrison, *J.*, 1957, 1439.
[9] Everest, *J.*, 1955, 4415.

equilibrium exists in these solutions between, on the one side, germanic acid or its dehydration product germanium dioxide, and, on the other side, chlorogermanate anions $GeCl_5^-$ or $GeCl_6^{2-}$, with one or more intermediate species represented by $[Ge(OH)_xCl_{5-x}]^-$. These intermediate species are the chief germanium species present in 6·5—9·0M-hydrochloric acid solutions, as is shown by the Ge : Cl ratios of the germanium chloro-complexes sorbed by the resin. Below 6·5M-hydrochloric acid hydrolysis of these intermediate species occurs with precipitation of germanium dioxide. Above 9M-hydrochloric acid chlorination of the intermediate species occurs with the formation of germanium tetrachloride as a separate phase. It is possible that chlorogermanate ions are formed initially in the latter reaction, but at the germanium concentrations used in this work the chlorogermanate ions rapidly decompose into germanium tetrachloride and chloride ions, thus explaining the decreased germanium solubilities observed with increased hydrochloric acid concentration (see Figure). Only in the sparingly soluble cæsium and rubidium hexachlorogermanates, and possibly in the very dilute solutions used by Yoshino [4] and by Nelson and Kraus,[5] do chlorogermanate ions exist as a stable or major species. However, the fact that cæsium and rubidium hexachlorogermanate can be precipitated from solutions of quadrivalent germanium in 7M-hydrochloric acid, indicates that an equilibrium concentration of chlorogermanate ions exists in these solutions, although their concentration is too low for detection by ion-exchange methods.

In the bromide system the low solubility of both germanium dioxide and tetrabromide in hydrobromic acid (see Figure), together with the negligible sorption of germanium from the solutions by ion-exchange resins, indicates that no germanium bromo-complexes are formed.

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343. *The Preparation and Examination of Organic Fluorine Compounds. Part XXIV.* The Halogenation of Fluorobenzene.*

By G. OLÁH, A. PAVLÁTH, and G. VARSÁNYI.

The directing effect of fluorine in fluorobenzene has been examined for (i) iron-catalysed chlorination and bromination, (ii) chlorination by iodine chloride and bromination by iodine bromide, and (iii) high-temperature radical halogenation. The isomer ratios in the radical high-temperature substitutions are not wholly accounted for by statistical distribution, influenced by the steric *ortho*-effect.

PREVIOUS authors have examined the halogenation of fluorobenzene by electrophilic reagents [1] and also its vapour-phase bromination. In the latter case the investigation was only qualitative and the isomer ratio could not be determined: Holleman thermogravimetric analysis was impossible because of the similarity of the physical constants of the products, and it was proved only that the amount of *meta*-isomer was substantially increased and that of the *para*-isomer decreased, whence complete analogy with the halogenation of chloro- and bromo-benzene was assumed.[3] Our investigations have concerned both the above types of halogenation of fluorobenzene.

Chlorination in presence of an iron catalyst gave 84% of *p*- and 16% of *o*-chlorofluorobenzene, the ratio being determined by means of ultraviolet-absorption vapour spectra.

In chlorination of fluorobenzene by electrophilic reagents, as in its nitration,[4] the *para*-orienting effect predominates. The following explanation can be offered: The negative

* Part XXIII, *J. Org. Chem.*, in the press.

[1] Schiemann and Pillarsky, *Ber.*, 1931, **64**, 1340; Varma, Venkataraman, and Nilkintiah, *J. Indian Chem. Soc.*, 1944, **21**, 112; Ferguson, Garner, and Mack, *J. Amer. Chem. Soc.*, 1954, **76**, 1251.

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inductive ($-I$) and the positive conjugative ($+K$) effect counteract each other, though the former is quantitatively the more powerful.[5] At the *ortho*-positions the two opposing effects are approximately equal; but in propagation through the ring the inductive effect weakens whilst the conjugative effect remains almost unchanged so that at the *para*-position the latter predominates and substitution occurs there.

Thus the fluorine substituent causes electronic deactivation at the *ortho*-positions. But this effect must not be confused with the steric *ortho*-effect which is lowest for fluorine, with its smallest van der Waals radius, of all the halogens. The steric effect, though smallest with fluorine, does however operate, as expected on theoretical grounds, for the amount of *ortho*-isomer formed decreases as the space-demand of an electrophilic substituent increases; for instance, we have found the following amounts of *ortho*-substitution of fluorobenzene: chlorination, 16%; nitration, 8%;[6] bromination, 1·8%; chlorosulphonation, *ca.* 1%.[7]

The electronic deactivating *ortho*-effect is clearly observed when second and third chlorine atoms are introduced on chlorination of fluorobenzene, for very little substitution occurs at the positions *ortho* to fluorine.[8]

Iron-catalysed bromination of fluorobenzene proceeds essentially similarly: monobromination gave 98·2% of *para*- and 1·8% of *ortho*-isomer, in line with the greater space-demand of the bromine cation. In a similar reaction, catalysed by aluminium bromide at 54—57° Ferguson, Garner, and Mack [1] found *ortho* 10·5%, *meta* 0·2%, and *para* 89·3%.

Hitherto iodine chloride has been known in preparative organic chemistry principally as an iodinating agent,[9] being generally used in glacial acetic acid. Lambourne and Robertson,[10] however, found that in a polar solvent one-fifth of the reaction was chlorination. We find that in a non-polar solvent, *e.g.*, carbon tetrachloride, or in absence of a solvent chlorination is the principal reaction, just as bromination is known to be with iodine bromide.[11] From fluorobenzene under these conditions there are formed 80% of chlorofluorobenzenes and less than 20% of fluoroiodobenzenes: at room temperature there is practically no iodination, and at 60° not more than 20%. Reaction in a polar solvent such as methanol or acetic acid gives mainly *p*-fluoroiodobenzene and no chlorofluorobenzene can be isolated.

Similarly, iodine bromide in carbon tetrachloride gives mainly bromofluorobenzenes and there is less than 5% of iodination.

The mechanism of action of these interhalogen compounds was studied by investigating the isomer ratios. Spectroscopic analysis of the chlorofluorobenzenes formed by iodine chloride in carbon tetrachloride gave the ratios: *ortho*, 6·1%; *meta*, 2·7%; *para*, 91·2%. The fluoroiodobenzene formed in methanol was the almost pure *para*-compound. Bromination with iodine bromide gave the ratios: *ortho*, 2·1%; *meta*, 1·8%; *para*, 96·1%. Comparison of these ratios with those obtained in the purely electrophilic iron-catalysed halogenations shows that here too substitution is purely electrophilic: nucleophilic substitution would have given mainly the *meta*-isomer.

Since iodine separates on chlorination with iodine chlorine whilst the issuing gases contain hydrogen chloride and no detectable amounts of hydrogen iodide, we propose the following reaction sequences:

$$(a)\ 2ICl \rightleftharpoons I_2 + Cl_2$$
$$(b)\ ICl + Cl_2 \rightleftharpoons Cl^+ + ICl_2^-$$
$$(c)\ ICl \rightleftharpoons I^+ + Cl^-$$
$$(d)\ I^+ + Cl_2 \rightleftharpoons ICl + Cl^+$$

The I^+ formed in reaction (*c*) accounts for the small amount of iodination, but most of this ion is used in the faster reaction (*d*) which, leading to Cl^+, accounts for the predominant chlorination. The separation of iodine is mainly due to a secondary reaction:

$$F{\cdot}C_6H_4{\cdot}H + ICl \longrightarrow p\text{-}F{\cdot}C_6H_4{\cdot}Cl + HI$$
$$HI + ICl \longrightarrow I_2 + HCl$$

A similar mechanism can be postulated for iodine bromide.

For free-radical halogenation of fluorobenzene we have used the high-temperature technique of Wibaut and his school.[2,3b] It is known that under these conditions, in the presence of first-order substituents, the proportion of *meta*-isomer is considerably greater. For instance, on bromination of bromobenzene Wibaut [2] found the *m*-dibromobenzene content of the product to be 25% at 380° rising to 60% at 630° while the *para*-content fell from 52% to 21%, the *ortho*-content remaining about constant (19—26%); he found similar results with chlorobenzene; and he assumed similar isomer distribution with fluorobenzene although in this case all he could determine was a decreased *para*-content at higher temperatures.

We have chlorinated and brominated fluorobenzene in the vapour phase in a smooth silica tube at 260—680° without a catalyst or carrier, with results shown in Table 1.

TABLE 1. *Halogenation of fluorobenzene in the vapour phase.*

C_6H_4BrF				C_6H_4ClF			
Temp.	*o*- (%)	*m*- (%)	*p*- (%)	Temp.	*o*- (%)	*m*- (%)	*p*- (%)
260°	1·8	6·4	91·8	260°	1·7	32·0	66·3
345	1·9	5·6	92·5	345	2·7	47·2	50·1
420	3·7	8·0	88·3	450	9·5	57·5	33·0
500	5·2	31·0	63·8	520	9·0	58·0	33·0
600	11·5	60·5	28·0	600	11·5	56·5	32·0
680	13·8	60·2	26·0	680	10·0	58·0	32·0

For radical-halogenation Wibaut suggests that at the high temperatures concerned the reactants have such high energy contents that differences in activation energy of the individual carbon atoms of the benzene ring do not influence the reaction velocities at these positions; he believes the isomer ratio to be determined statistically. Since in a monosubstituted benzene there are two *ortho*-, two *meta*-, and one *para*-position the isomer distribution should thus be *ortho* 40%, *meta* 40%, and *para* 20%. That there is less *ortho*- and more *meta*-isomer in practice is attributed by Wibaut to steric hindrance at the *ortho*-position. Now the fluorine in fluorobenzene has a relatively small atomic volume,

TABLE 2. *Amounts* (%) *of* ortho-*substitution of halogenobenzenes.*

		PhF	PhCl	PhBr	PhI
Chlorination :	electrophilic	16·0	39·0	45·1	—
	radical	11·5	15·0	—	—
Nitration :	electrophilic	8·0	30·1	37·6	43·3
	radical	38·0	—	—	—
Bromination :	electrophilic	1·8	11·2	13·1	18·2
	radical	11·5	18·0	20·0	—

so on Wibaut's hypothesis fluorobenzene should give more *ortho*-isomer than bromobenzene; but, as shown above, the reverse is found experimentally for chlorination and bromination. Similar contradictions of the hypothesis are found in other reactions of halogenobenzenes, as shown in Table 2. The decrease in the amount of *ortho*-substitution must therefore be attributed mainly to energetic causes and in no case solely to steric

[2] Wibaut, *Experientia*, 1949, **5**, 340.

[3] (*a*) Wibaut, van de Lande, and Wallagh, *Rec. Trav. chim.*, 1933, **52**, 794; 1937, **56**, 65; (*b*) van Loon and Wibaut, *ibid.*, 1937, **56**, 815.

[4] Holleman, *ibid.*, 1903, **23**, 261; Swartz, *ibid.*, 1913, **33**, 263.

[5] Bird and Ingold, *J.*, 1938, 918.

[6] Oláh and Pavláth, *Acta Chim. Acad. Sci. Hung.*, 1954, **4**, 111.

[7] Oláh, Pavláth, Kuhn, and Varsányi, *ibid.*, 1955, **7**, 431, and unpublished results.

[8] *Idem, Tagungsber. Chem. Ges. D.D.R*, 1955, in the press; Oláh and Pavláth, "Vegyipari Kutató Intézetek Közleményei," Vol. IV, p. 48.

[9] Sandin, Drake, and Leger, *Org. Synth.*, Coll. Vol. II, p. 196; Woollett and Johnson, *ibid.*, p. 343; Wallingford and Krueger, *ibid.*, p. 349.

[10] Lambourne and Robertson, *J.*, 1947, 1167.

[11] Militzer, *J. Amer. Chem. Soc.*, 1938, **60**, 256.

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causes. Although Wibaut's hypothesis is thus not fully adequate it remains true that the relatively high heat-energy of the molecules in high-temperature reactions must play a substantial part in determining orientation.

Recently the orientation in radical reactions has been explained in terms of the free-valency theory introduced by molecular-orbital considerations.[12] The free valency gives information about the electron distribution of the conjugated systems, and its value is in some measure characteristic of the binding power of the individual carbon atoms. In radical reactions the radical has for disposal one uncompensated electron which " attempts " to be incorporated into a bond with compensation of spin; and the greater the free valency of a carbon atom the greater is its disposition for reaction with the uncompensated electron. However, Hey and Williams,[13] using bond orders given by Sandorfy,[14] calculated the free valencies for halogenobenzenes, which indicate the order $o > p > m$, so that the observed isomer ratios cannot be explained by free valency alone.

Previous authors have paid no attention to Coulomb forces on the grounds that neutral radicals were under consideration. But some neutral radicals possess dipole moments, and in these cases their interaction with the free charges appearing on the atoms of the ring will increase or decrease the activation energy. Moreover, even radicals, such as those from halogen atoms, which have no dipole moment when alone, will become polarized under the influence of the charges on the ring atoms. Thus neutral radicals will in fact be subject to Coulomb forces, which will vary from one position in the ring to another, being greatest where the free charge is greatest. For the halogenobenzenes the largest free charges are at the *meta*-positions, usually about $0{\cdot}10$—$0{\cdot}14 \times 10^{-10}$ unit, the values at the *para*- and the *ortho*-positions being about one-third of these. *E.g.*, Ri and Eyring [15] have calculated the charge distribution as follows:

	PhF	PhCl	PhBr	PhI
ortho	0·0363	0·0473	0·0446	0·0194
meta	0·0933	0·115	0·116	0·0909
para	0·00351	0·0271	0·0305	0·00651

We conclude that the orientation in high-temperature halogenations is due to three factors: (1) The high energy content of the radical favours statistical distribution. (2) Owing to interaction with the uncompensated electrons of the radicals the free valencies at the ring carbon atoms contribute to changes in the activation energy, higher free valency lowering the activation energy and thus increasing the proportion of substitution at that position. (3) Neutral radicals, whether they have normally a dipole moment or whether polarisation is induced by the free charge appearing at ring carbon atoms, will be influenced by that free charge; the greater the free charge, the greater is the amount of substitution at that position.

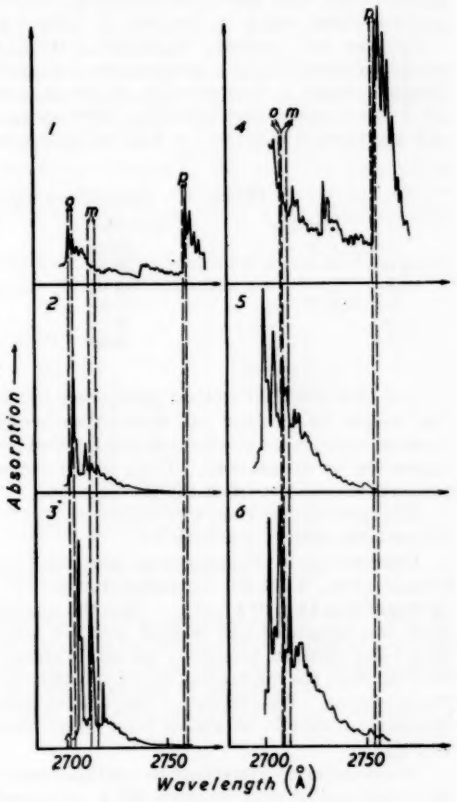
Experimental

Determination of the Isomer Ratios in Chloro- and Bromo-fluorobenzene.—Ultraviolet absorption spectra have often been used for analysis of aromatic compounds,[16] but the differences in extinction are not great for solutions so that errors tend to be large. We have determined the isomer ratio for chloro- and bromo-fluorobenzene by means of the ultraviolet absorption spectra of the vapour in equilibrium with the liquid. The composition of the vapour mixture then yields that of the liquid by application of Raoult's and Henry's laws. Alternatively the composition of the liquid phase can be determined directly if, in place of

[12] Coulson, *J. Chim. phys.*, 1948, **45**, 243; Daudel and his co-workers, *Bull. Soc. chim. France*, 1950, **17**, 66; Longuet-Higgins and his co-workers, *Trans. Faraday Soc.*, 1951, **47**, 553.
[13] Hey and Williams, *Discuss. Faraday Soc.*, 1953, **14**, 216.
[14] Sandorfy, *Bull. Soc. chim. France*, 1949, **16**, 615.
[15] Ri and Eyring, *J. Chem. Phys.*, 1940, **8**, 433.
[16] *E.g.*, Fry, Nusbaum, and Randall, *J. Appl. Chem.*, 1946, **17**, 150; Nielsen and Smith, *Ind. Eng. Chem. Anal.*, 1943, **15**, 609; Robertson, Ginsburg, and Matsen, *ibid.*, 1946, **18**, 746.

molar extinction coefficients, the absorption coefficients of the saturated vapours of the pure components at the appropriate temperature are used :[17] $\beta = (\log I_0/I)/d$, where d is the layer thickness (in mm.).

Having the vapour spectra of the pure components we did not measure actual extinctions but only differences in the extinction at neighbouring points of the spectra, choosing as " analytical pair " a sharp maximum for the particular isomer and its adjacent minimum.



Wavelengths of " analytical pairs " used in analysis of isomeric mixtures of chloro- and bromo-fluorobenzene (cf. Table 3).

C_6H_4BrF : 1, *p*-; 2, *o*-; 3, *m*-.
C_6H_4ClF : 4, *p*-; 5, *o*-; 6, *m*-.

We then change the above formula to $\Delta\beta = (\log I_1/I_2)/d$, where I_1 and I_2 are the intensities for the analytical pair.[18]

The Figure shows the vapour spectra of the isomeric chloro- and bromo-fluorobenzenes and the analytical pairs where the difference in optical density provides the values of I_1/I_2. The quantitative data for these pairs are in Table 3.

TABLE 3. *log* I_1/I_2 *for the isomers.*

	C_6H_4ClF; d = 22 mm.; 10°				C_6H_4BrF; d = 53 mm.; 10°			
	λ (Å)	*o*	*m*	*p*	λ (Å)	*o*	*m*	*p*
ortho-Pair	2708·5—2707·9	0·286	−0·020	−0·003	2703·4—2701·2	1·129	0·070	−0·135
meta-Pair	2711·5—2708·5	−0·081	0·435	−0·061	2711·0—2714·7	0·061	1·000	0·035
para-Pair	2755·6—2754·0	0·001	−0·007	1·022	2760·0—2758·4	0·005	−0·005	0·992

For the chlorofluorobenzenes the analytical pair for the *para*-isomer corresponds to the 0–0 transition, and for the *ortho*- and *meta*-isomer to the 2–2 transition of the lower-frequency

[17] Oláh, Pavláth, Kuhn, and Varsányi, *Acta Chim. Acad. Sci. Hung.*, 1955, **7**, 431.
[18] Vaughn and Stearn, *Analyt. Chem.*, 1949, **21**, 1361.

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normal vibration concomitant to the 0–0 transition. For the bromofluorobenzenes the analytical pairs for the *ortho*- and the *para*-isomer correspond to the 0–0 transition, and for the *meta*-isomer to the 1–1 transition of a lower-frequency vibration; however, in place of the 0–0 transition for the *ortho*-isomer there is a maximum of an intense band due to the *para*-isomer and corresponding to a 0–1 transition of a C–X vibration.

The experimental error in recording and reading each point of an analytical pair was 0·003, in conformity with previous experience. Since there are two points, the maximum error for a pair was 0·006, which on the basis of Table 3 gives the following maximum errors: C_6H_4ClF, *o*- 2·1%, *m*- 1·4%, *p*- 0·6%; C_6H_4BrF, *o*- 0·5%, *m*- 0·6%, *p*- 0·6%. The error due to presence of other components is of a lower order of magnitude: *e.g.*, for determination of *o*-chlorofluorobenzene, errors in determination of the *meta*-isomer cause an error of (0·006/0·435) × 100% (cf. Table 3), which, multiplied by 0·020, causes an error of ~0·0003 in log I_0/I. The accuracy of the analysis is illustrated in Table 4 which gives results for four known mixtures.

TABLE 4. *Analysis of mixtures of known composition.*

Isomer	Compn. (%)	Found (%)	Compn. (%)	Found (%)
o-C_6H_4ClF	62·43	62	28·92	29·5
m- ,, ...	25·55	25	56·40	56
p- ,, ...	12·02	13	14·68	14·5
o-C_6H_4BrF	61·59	62	24·09	23·5
m- ,, ...	30·11	30·5	51·82	51·5
p- ,, ...	8·30	7·5	24·09	25·0

Our spectroscopic method determines the relative amounts of the isomers. In obtaining the sample for analysis we removed unchanged fluorobenzene and then isolated the mixed isomeric substitution products in one fraction (the b. p.s of the isomers are too similar to permit separation by distillation). Thus, in our method, if there is any loss in the isolation of the products it does not affect the isomer ratio.

The spectral bands are well separated, and the final error in the determination never exceeds 2% and is in general less than 1%.

Chlorination of Fluorobenzene with an Iron Catalyst.—Chlorine was passed into fluorobenzene (48 g., 0·5 mole) containing iron powder, with stirring and ice-cooling, until the increase in weight was 14 g. (0·4 mole). Then the mixture was steam-distilled, and the volatile organic layer was separated and washed with 5% aqueous sodium hydroxide and then with water, dried, and distilled through a 40 cm. Widmer column. After removal of unchanged fluorobenzene (6 g.) the residue was shown spectroscopically to contain 16% of *o*- and 84% of *p*-chlorofluorobenzene. Distillation of the residue gave a fraction (42 g.), b. p. 129—131°, shown spectroscopically to be almost pure *para*-isomer (Found: Cl, 28·0. Calc. for C_6H_4ClF: Cl, 27·2%).

Bromination of Fluorobenzene with an Iron Catalyst.—Bromine (64 g., 0·4 mole) was added to stirred, cooled fluorobenzene (48 g., 0·5 mole) containing iron powder (1 g.). The mixture was heated on the water-bath until evolution of hydrogen bromide ceased (~1 hr.), then distilled in steam and worked up as before, giving unchanged fluorobenzene (4 g.) and a residue shown spectroscopically to contain 98·2% of *p*- and 1·8% of *o*-bromofluorobenzene. Distillation gave almost pure *para*-isomer (62 g.), b. p. 151—153° (Found: Br, 45·3. Calc. for C_6H_4BrF: Br, 45·8%).

In this and the preceding experiment the amount of *meta*-isomer was less than the experimental error (1%).

Reaction of Fluorobenzene with Iodine Chloride.—(*a*) Iodine chloride (40·5 g., 0·25 mole) in carbon tetrachloride (200 ml.) was added to stirred, cooled fluorobenzene (24 g., 0·25 mole), then the whole was refluxed for 10 hr. Iodine was filtered off, and the filtrate washed with 10% aqueous sodium carbonate until neutral and then with aqueous sodium thiosulphate until free from residual iodine, dried ($CaCl_2$), and distilled. After removal of carbon tetrachloride and fluorobenzene, a fraction (5·5 g.), b. p. 125—135° (Found: Cl, 27·6%), was obtained and shown spectroscopically to contain *p*- 91·2%, *o*- 6·1%, and *m*-chlorofluorobenzene 2·7%. No dichloro-derivative could be isolated. The distillation residue contained 0·5 g. of fluoroiodobenzene.

(*b*) Similar amounts of reactants in dry methanol (150 ml.) were refluxed for 5 hr., then after

removal of most of the solvent by distillation were worked up as in (*a*). No chlorofluorobenzene was obtained but, instead, *p*-fluoroiodobenzene, b. p. 180—185° (Found : I, 56·45. Calc. for C_6H_4IF : I, 57·15%).

Reaction of Fluorobenzene with Iodine Bromide.—Iodine bromide (52 g., 0·25 mole) in carbon tetrachloride (250 ml.) was added with stirring and cooling to fluorobenzene (24 g., 0·25 mole) in carbon tetrachloride (50 ml.). After being kept at 50° for 5 hr. the mixture was worked up as in the experiments with iodine chloride to give fractions, (i) b. p. 148—152° (6·2 g.), shown spectroscopically to contain 96·1% of *p*-, 2·1% of *o*-, and 1·8% of *m*-bromofluorobenzene (Found : Br, 45·2%), and (ii) *p*-fluoroiodobenzene, b. p. 182—185° (Found : I, 56·7%).

Chlorination of Fluorobenzene in the Vapour Phase.—Reaction was carried out in a smooth, transparent silica tube (1 m. long, 25 mm. in diameter) heated in a vertical electric furnace for 75 cm. of its length. The temperature variation of the furnace was 6—8° at 600° and 2—3° at 400°. Fluorobenzene was dropped into an evaporator at 120° and mixed at that temperature with a chlorine stream passing at a rate of 20 l./hr. for reaction up to 345° or 4 l./hr. for reaction at >450°. The gases issuing from the reaction tube were condensed in acetone–carbon dioxide, distilled in steam, washed with aqueous alkali and water, dried ($CaCl_2$), and distilled through a 40 cm. Widmer column.

Isomer ratios for the products are given in Table 1. Other details are in Table 5 and refer to 0·5 mole of fluorobenzene. There was no reaction at room temperature.

TABLE 5. *Chlorinations.*

Temp.	Time of reaction (min.)	Product g.	Product b. p.	Residue after steam-distn. (g.)
260°	48	1·5	125—132°	—
345	43	1·6	125—131	—
450	35	3·1	122—128	0·5
520	33	3·3	,,	0·4
600	30	4·1	123—129 *	2·1
680	36	3·8	124—130 †	2·5

* Also a fraction (1·9 g.), b. p. 155—163°, probably dichlorofluorobenzenes (Found : Cl, 42·6. Calc. for $C_6H_3Cl_2F$: Cl, 43·0%).

† Also a fraction (2·5 g.), b. p. 158—164°, probably dichlorofluorobenzenes (Found : Cl, 42·7%).

Bromination of Fluorobenzene in the Vapour Phase.—The apparatus was that used for chlorination. Bromine vapour was mixed at 80° with the fluorobenzene by means of a stream of nitrogen at 30 l./hr. Unchanged bromine was removed from the products by washing them with aqueous sodium thiosulphate; otherwise working up was as for chlorination.

Isomer ratios for the products are given in Table 1. Other details are in Table 6 and refer to 0·5 mole of fluorobenzene.

TABLE 6. *Brominations.*

Temp.	Br (g.)	Time (min.)	Product g.	Product b. p.	Residue after steam-distn.
260°	40	48	2·1	150—152°	—
345	44	<46	2·7	149—152	—
420	64	42	3·2	150—153	—
500	36	32	14·2	148—152	3·5 g., tar
600	36	50	16·3	149—153	5·2 g.
680	32	50	14·9	148—152	9·5 g., tar

CHEMICAL CENTRAL RESEARCH INSTITUTE OF THE HUNGARIAN ACADEMY OF SCIENCES, BUDAPEST, XIV, HUNGÁRIA-KRT. 114. [*Received, June 1st,* 1956.]

344. *Pyrimidines. Part IX.* The Ultraviolet Absorption Spectra of the Isomeric* O : 6- *and* N : 6-*Dimethyluracils.*

By J. F. W. McOmie, E. R. Sayer, and (in part) J. Chesterfield.

The ultraviolet absorption spectra of the compounds named in the title are discussed. Thermal isomerisation of 4-hydroxy-2-methoxy-6-methyl- and of 2-hydroxy-4-methoxy-6-methyl-pyrimidine yields 3 : 6- and traces of 1 : 6-dimethyluracil respectively, together with some 6-methyluracil.

In the ultraviolet absorption spectra [1,2] of mono- and of poly-substituted pyrimidines containing not more than one potentially tautomeric group, the effect of the individual substituents on both the wavelength of maximum absorption and the extinction coefficient is approximately additive. In general the calculated values for $\lambda_{max.}$ agreed with those observed within 6 mμ (mostly within 4 mμ), unless steric hindrance prevented coplanarity of the substituent with the pyrimidine ring. However, the predicted wavelength [2] (286·5 mμ) for 4-hydroxy-2-methoxy-6-methylpyrimidine was greatly different at pH 13 from that observed [3] (263 mμ) and it was considered possible that the *O*-methyl group had migrated to one of the nitrogen atoms, under the action of the aqueous alkali or of ultraviolet light (during the measurement of the spectrum); it is known that the compound undergoes thermal isomerisation.[3] The first alternative was disproved when it was found that the 2-methoxy-compound could be recovered after one hour in solution in alkali. The alternative was investigated by studying the spectra of the isomeric *N* : 6-dimethyluracils.

Direct methylation of 6-methyluracil gives a difficultly separable mixture of 1 : 6- and 3 : 6-dimethyl- and 1 : 3 : 6-trimethyl-uracil.[4] The pure 3 : 6-dimethyl compound was made by Wheeler and McFarland's method,[5] *i.e.*, by methylating 4-hydroxy-6-methyl-2-methylthiopyrimidine with methyl iodide and hydrolysing the resulting 3 : 4-dihydro-3 : 6-dimethyl-2-methylthio-4-oxopyrimidine with concentrated hydrochloric acid. Methylation of 2 : 4-dimethoxypyrimidine is known to give 1 : 2-dihydro-1-methyl-4-methoxy-2-oxopyrimidine which can be hydrolysed to 1-methyluracil [6] and we have used the same reagents to convert 2 : 4-dimethoxy-6-methylpyrimidine into 1 : 6-dimethyluracil in good yield.

Compound	pH of aq. soln.	$\lambda_{max.}$ (mμ)	$\log_{10}\varepsilon$	$\lambda_{min.}$ (mμ)	$\log_{10}\varepsilon$
4-Hydroxy-2-methoxy-6-methylpyrimidine	13	222	3·85	242	3·51
		(222 *)	(3·83 *)		
		263	3·88		
		(263 *)	(3·87 *)		
2-Hydroxy-4-methoxy-6-methylpyrimidine	13	222	4·01	246	3·24
		275·5	3·91		
1 : 6-Dimethyluracil	13	265	3·90	241	3·48
3 : 6-Dimethyluracil	13	220	3·85	245	2·98
		280·5	4·07		
The 4-hydroxy-compound after thermal isomerisation	13	219	3·91	245	3·20
		280·5	4·07		
6-Methyluracil	13	277	3·83 *		
4-Methoxypyrimidine	6·95	247·5	3·53 †	—	—
,,	Ethanol	248	3·45	—	—

* Quoted from ref. 3. † Quoted from Brown, Hoerger, and Mason, *J.*, 1955, 211.

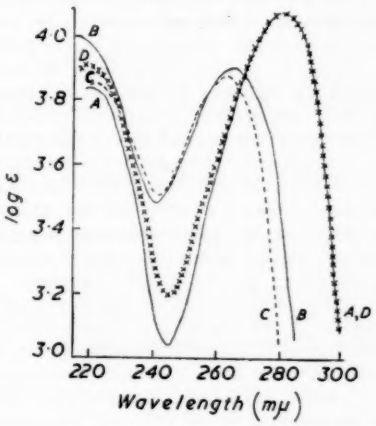
The ultraviolet absorption spectra of the pyrimidines under discussion are shown in the Table and the Figure. The spectrum of 4-hydroxy-2-methoxy-6-methylpyrimidine

* Part VIII, *J.*, 1955, 3478.

[1] Boarland and McOmie, *J.*, 1952, 3716.
[2] *Idem, ibid.*, p. 3722.
[3] Marshall and Walker, *J.*, 1951, 1004.
[4] Behrend and Thurm, *Annalen*, 1902, **322**, 165.
[5] Wheeler and McFarland, *Amer. Chem. J.*, 1909, **42**, 101.
[6] Hibbert and Johnson, *J. Amer. Chem. Soc.*, 1930, **52**, 2001.

at pH 13 agreed with that recorded by Marshall and Walker;[3] it is different from those of 1 : 6- and 3 : 6-dimethyluracil even though it closely resembles that of the former (see Figure); and we conclude that no rearrangement occurred during the measurement of its spectrum. The difference between the observed and the predicted $\lambda_{max.}$ for the 4-hydroxy-compound ($\Delta\lambda = -23{\cdot}5$ mμ) is comparable with that for compounds containing two potentially tautomeric groups, *e.g.*, 2-amino-4-hydroxypyrimidine at pH 13 has $\lambda_{max.}$ at 273 mμ,[7] whereas the predicted value would be 313·5 mμ. Other methoxypyrimidines are also anomalous: 2 : 4-dimethoxypyrimidine (in ethanol)[8] has $\lambda_{max.}$ 258 mμ (predicted 271·5 mμ) and 2 : 4 : 6-trimethoxypyrimidine[9] at pH 5·0—13 has $\lambda_{max.}$ 248 mμ (predicted 273 mμ), while 4-amino-2-methoxypyrimidine[10] at pH 7·2 has $\lambda_{max.}$ 270·5 mμ (predicted 289 mμ).

Recently[11] the additivity rule was found to apply to derivatives of pyridazine and of pyridaz-6-one which contained not more than one strongly inductive or conjugative substituent. The two isomeric 4-methoxypyridazines and the one 4-methoxypyridaz-6-one examined gave anomalous results and the 4-methoxy-group appeared to act as a strongly inductive or conjugative group. In the pyrimidine series the 2-methoxy-group causes a bathochromic shift of 21 mμ (23·5 in ethanol), whereas the 4-methoxy-group (see Table) produces a shift of only 4·5 mμ (4 in ethanol); nevertheless, the predicted $\lambda_{max.}$ (295·5 mμ) for 2-hydroxy-4-methoxy-6-methylpyrimidine at pH 13 does not agree with that observed (275·5 mμ), and it must be concluded that the additivity rule does not apply to pyrimidines containing a 2- or 4-methoxy-group as well as a potentially tautomeric substituent, nor does it apply to 2 : 4-di- or 2 : 4 : 6-tri-methoxypyrimidine.



Absorption spectra of:
A, 3 : 6-*Dimethyluracil.*
B, 1 : 6-*Dimethyluracil.*
C, 4-*Hydroxy-2-methoxy-6-methylpyrimidine.*
D, *The latter after thermal rearrangement.*

2-Hydroxy-4-methoxy-6-methylpyrimidine was made by taking advantage of the reactivity of the 2-methylsulphonyl group of 4-methoxy-6-methyl-2-methylsulphonylpyrimidine (cf. ref. 12), itself prepared by the action of chlorine on an ice-cold aqueous suspension of 4-methoxy-6-methyl-2-methylthiopyrimidine. The 2-methylsulphonyl group has about the same reactivity as that of the 2-chloro-group, and, like many chloropyrimidines, the 2-methylsulphonyl compound was lachrymatory and vesicant. Alkaline hydrolysis of the 2-methylsulphonyl compound gave the desired 2-hydroxy-4-methoxy-6-methylpyrimidine. During the work, the latter compound was described by Ochiai and

[7] Stimson and Reuter, *ibid.*, 1945, **67**, 2191.
[8] Austin, *ibid.*, 1934, **56**, 2141.
[9] Shugar and Fox, *Bull. Soc. chim. belg.*, 1952, **61**, 44.
[10] *Idem*, *Biochim. Biophys. Acta*, 1952, **9**, 199.
[11] Eichenberger, Rometsch, and Druey, *Helv. Chim. Acta*, 1954, **37**, 1298.
[12] Andrews, Anand, Todd, and Topham, *J.*, 1949, 2490.

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Yamanaka [13] who made it by the action of toluene-*p*-sulphonyl chloride, followed by 10% aqueous potassium carbonate, on the *N*-oxide of 4-methoxy-6-methylpyrimidine.

That 4-hydroxy-2-methoxy-6-methylpyrimidine is isomerised by heat has been noted previously [3] and we have now shown that the product is 3 : 6-dimethyluracil, together with a little 6-methyluracil. Similar isomerisation of 2-hydroxy-4-methoxy-6-methylpyrimidine did not proceed smoothly and the chief product was 6-methyluracil. In some experiments traces of 1 : 6-dimethyluracil were obtained. Both 3 : 6- and 1 : 6-dimethyluracil were unchanged when heated under the conditions used for isomerisation of the methoxypyrimidines. The rearrangement of the 4-methoxy-compound is probably intermolecular and is in contrast with that of 4-methoxypyrimidine itself which readily yields 1 : 6-dihydro-1-methyl-6-oxopyrimidine.[14]

Experimental

1 : 6-*Dimethyluracil*.—2 : 4-Dimethoxy-6-methylpyrimidine [15] (2 g.) in methyl iodide (30 ml.) was kept for 3 days at room temperature. The solvent was evaporated, N-hydrochloric acid (50 ml.) was added, and after 1·5 hr. the solution was made neutral and evaporated to dryness (water-bath). Extraction of the residue with chloroform yielded 1 : 6-dimethyluracil (1·5 g., 82%), m. p. 218—220°, raised by recrystallisation from water to m. p. 220° alone or mixed with an authentic sample kindly supplied by Dr. W. Hepworth [16]

Thermal Isomerisation of **4-*Hydroxy*-2-*methoxy*-6-*methylpyrimidine*.**—The 2-methoxy-compound (500 mg.) was packed into capillary m. p. tubes so that each contained about 0·5 in. of solid. These tubes were packed fairly tightly into a test-tube which was then heated in an oil-bath at the rate of 5°/min. The compound melted at 190—195° and partly resolidified; heating was continued at 205—208° for 10 min. After having been cooled, the capillary tubes were crushed and the pale brown residue extracted with boiling water (40 ml.). The aqueous extract was treated with charcoal and evaporated to *ca.* 3 ml., from which there separated needles (300 mg.), m. p. 255—260° (decomp.). After recrystallisation from water, they melted at 263—265° (decomp.). This compound was shown to be identical with 3 : 6-dimethyluracil by mixed m. p., the similarity of their spectra (see Figure), and by paper chromatography.

With solvent A (benzene–ethanol–water, 169 : 45 : 15 by vol.) the product gave two spots, when viewed under ultraviolet light, consisting of 3 : 6-dimethyluracil (R_F 0·49) and 6-methyluracil (R_F 0·08); no starting material (R_F 0·65) could be detected. With solvent B (*tert.*-butyl alcohol–benzene–water, 60 : 15 : 45) the product showed 6-methyluracil (R_F 0·63) and a spot at R_F 0·85 of 3 : 6-dimethyluracil and/or starting material.

4-*Chloro*-6-*methyl*-2-*methylthiopyrimidine*.—4-Hydroxy-6-methyl-2-methylthiopyrimidine (25 g.), phosphoryl chloride (160 ml.), and dimethylaniline (10 ml.) were boiled under reflux for 1·5 hr. The chloropyrimidine was isolated in the usual way and sublimed at 100° (bath-temp.)/25 mm., giving needles (21 g., 75%), m. p. 37—38° (lit.,[17] m. p. 39—40°).

4-*Methoxy*-6-*methyl*-2-*methylthiopyrimidine*.—The above chloropyrimidine and a solution from sodium (2 g.) in methanol (100 ml.) were boiled under reflux for 3 hr. After being cooled and filtered, the solution was distilled, giving an oil (13·3 g., 91%), b. p. 125—130°/12 mm., which crystallised (lit.,[18] b. p. 126—130°/18 mm., m. p. 137—139°).

4-*Methoxy*-6-*methyl*-2-*methylsulphonylpyrimidine*.—The above 2-methylthio-compound (3·7 g.), suspended in water (40 ml.), was cooled in ice-water, and chlorine rapidly bubbled in until all the methylthio-compound had dissolved. Meanwhile the 2-methylsulphonylpyrimidine had begun to separate and was collected. A further crop was obtained by extracting the aqueous solution with chloroform. The total *product* recrystallised from 1 : 1 (v/v) chloroform–light petroleum (b. p. 60—80°) and then had m. p. 80° (yield, 3·2 g.) (Found: C, 39·5; H, 4·7; N, 13·6. $C_7H_{10}O_3N_2S$ requires C, 41·5; H, 4·95; N, 13·85%).

2-*Hydroxy*-4-*methoxy*-6-*methylpyrimidine*.—The methylsulphonyl compound (1·0 g.) rapidly dissolved in 10% aqueous sodium hydroxide (4 ml.) on the water-bath. Water (1 ml.) was

[13] Ochiai and Yamanaka, *Pharm. Bull.* (*Japan*), 1955, **3**, 175.
[14] Brown, Hoerger, and Mason, *J.*, 1955, 211.
[15] Gabriel and Colman, *Ber.*, 1901, **32**, 2921.
[16] Ainley, Curd, Hepworth, Murray, and Vasey, *J.*, 1953, 59.
[17] Wheeler and McFarland, *Amer. Chem. J.*, 1909, **42**, 435.
[18] Matsukawa and Shirakawa, *J. Pharm. Soc. Japan*, 1951, **71**, 933.

then added and heating continued for 0·5 hr. The mixture was cooled, then neutralised with dilute hydrochloric acid, and the solid collected and recrystallised from ethanol. The 2-hydroxy-4-methoxy-6-methylpyrimidine (0·3 g.) had m. p. 210—212° (Found : C, 51·4; H, 6·1; N, 19·9; OMe, 21·2. Calc. for $C_6H_8O_2N_2$: C, 51·5; H, 5·7; N, 20·0; OMe, 22·0%) (lit.,[12] m. p. 209—211°).

Thermal Isomerisation of 2-Hydroxy-4-methoxy-6-methylpyrimidine.—The 4-methoxypyrimidine (50 mg.) was heated in m. p. tubes at a rate of *ca.* 3°/min. up to 195° and kept at this temperature for 10 min. The dark brown residue was extracted with hot ethanol, and the solution (charcoal) concentrated to 0·5 ml. Light petroleum (b. p. 40—60°) was added and the precipitate (12 mg.) collected. On a paper chromatogram, solvent A (see above) showed the presence of starting material, and of 1 : 6-dimethyluracil and 6-methyluracil whose rates of movement *relative to that of the starting material* were 0·61 and 0·18, severally; solvent B showed spots of starting material (R_P 0·69), 1 : 6-dimethyluracil (R_P 0·58), and of 6-methyluracil (R_P 0·53). No trace of 3 : 6-dimethyluracil (relative rate of movement in solvent A 0·98 and R_P in solvent B 0·78) was found. In some experiments, no 1 : 6-dimethyluracil could be detected and 6-methyluracil was always the main product.

THE UNIVERSITY, BRISTOL. [*Received, November 9th,* 1956.]

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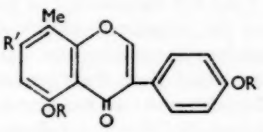
345. 5 : 4′-*Dihydroxy*-8-*methyl*isoflavone, *and a Note on Lotoflavin.*

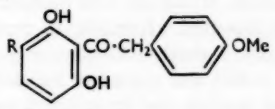
By W. B. WHALLEY.

The *iso*flavone named in the title has been synthesised and is not identical with " tatoin " from soya-beans.

THE isolation from soya-beans of three substances which were formulated as 5 : 7 : 4′-trihydroxy-8-methyl-, 5 : 7 : 2′-trihydroxy-8-methyl-, and 5 : 7 : 2′-trihydroxy-*iso*flavone, has been reported by Okano and Beppu.[1] The synthesis of the two *C*-methyl*iso*flavones[2] and of 5 : 7 : 2′-trihydroxy*iso*flavone[2,3,4] has conclusively demonstrated the inaccuracy of this claim whilst doubt has been expressed[3] about the identity of a fourth substance,



(I)



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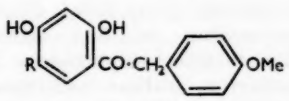

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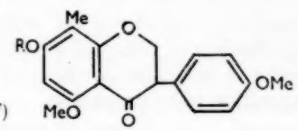

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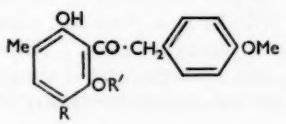

(V)

" tatoin," isolated from the same source by Okano and Beppu[1] and by Bhandari, Bose, and Siddiqui,[5] and formulated as 5 : 4′-dihydroxy-8-methyl*iso*flavone (I; R = R′ = H). The synthesis of this *iso*flavone is now described.

Condensation of *p*-methoxyphenylacetyl chloride with methyl 2 : 4-dihydroxy-5-methylbenzoate furnished the requisite 2 : 6-dihydroxy-4′-methoxy-5-methoxycarbonyl-3-methyldeoxybenzoin (V; R = CO_2Me, R′ = H), which was simultaneously hydrolysed

[1] Okano and Beppu, *J. Agric. Chem. Soc. Japan,* 1939, **15**, 645; *Chem. Abs.*, 1940, **34**, 429.
[2] Whalley, *J. Amer. Chem. Soc.*, 1953, **75**, 1059.
[3] Baker, Harborne, and Ollis, *J.*, 1953, 1860.
[4] Karmarkar, Shah, and Venkataraman, *Proc. Indian Acad. Sci.*, 1952, **36**, *A*, 552.
[5] Bhandari, Bose, and Siddiqui, *J. Sci. Ind. Res. India*, 1949, **8**, *B*, 217; *Chem. Abs.*, 1950, **44**, 3987.

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and decarboxylated to yield 2 : 6-dihydroxy-4′-methoxy-3-methyldeoxybenzoin (V; R = R′ = H), the orientation of which follows from the method of preparation, the characteristic green ferric reaction, and the non-identity with the isomeric 2 : 4-dihydroxy-4′-methoxy-5-methyldeoxybenzoin (III; R = Me). Monomethylation of the deoxybenzoin (V; R = R′ = H) furnished the expected monohydric phenol (V; R = H, R′ = Me) which was converted by standard methods into 5 : 4′-dihydroxy-8-methyl-*iso*flavone (I; R = R′ = H) the orientation of which, and hence of the cognate derivatives, was unequivocally established by the isolation of 2-hydroxy-4-methoxytoluene from fusion of the dimethyl ether (I; R′ = H, R = Me) with potassium hydroxide.

The properties of 5 : 4′-dihydroxy-8-methyl*iso*flavone and of the derivatives clearly establish its non-identity with Okano and Beppu's [1] "tatoin" and we are inclined to the view of Baker *et al.*[3], that "tatoin" is most likely identical with daidzein. Melting points of derivatives are as follows :

		Diacetate	Dimethyl ether
"Tatoin" (Okano and Beppu [1])	318°	185°	165°
,, (Bhandari *et al.*[3])	316—317	185	—
5 : 4′-Dihydroxy-8-methyl*iso*flavone	180	174	137

Many abortive routes were explored. 2 : 6-Dihydroxy-4′-methoxydeoxybenzoin (II; R = H) (an obvious key intermediate) could not be prepared from 2 : 6-dimethoxybenzonitrile and *p*-methoxybenzylmagnesium bromide since, as expected, 1 : 2-di-(*p*-methoxyphenyl)ethane was the only product, whilst *p*-methoxyphenylacetyl chloride and methyl 4 : 6-dihydroxy*iso*phthalate failed to react (cf. the successful use [4] of phenylacetyl chloride in this reaction). The condensation, under Friedel–Crafts conditions, of *p*-methoxyphenylacetyl chloride and methyl 2 : 4-dihydroxybenzoate furnished no detectable quantity of the ester (II; R = CO_2Me) (cf. *inter al.*, Naik, Thakor, and Shah [6]), but gave the isomeric 2 : 4-dihydroxy-4′-methoxy-5-methoxycarbonyldeoxybenzoin (III; R = CO_2Me), the orientation of which was established by decarboxylation to 2 : 4-dihydroxy-4′-methoxydeoxybenzoin (III; R = H). Furthermore, the hydrogenolysis of the toluene-*p*-sulphonates of phenols with Raney nickel which has been exploited in the flavone series (cf. *inter al.*, Akluwalia, Mukerjee, and Seshadri [7]) for the elimination of the 7-hydroxyl group failed, despite repeated attempts, to replace the toluene-*p*-sulphonyloxy-residue in 5 : 4′-dimethoxy-8-methyl-7-toluene-*p*-sulphonyloxy*iso*flavone (I; R′ = toluene-*p*-sulphonyloxy, R = Me) and gave two substances which from their general properties, analyses, and infrared spectra are formulated as 7-hydroxy-5 : 4′-dimethoxy-*iso*flavanone (IV; R = H) and the corresponding toluene-*p*-sulphonate (IV; R = toluene-*p*-sulphonyl).

Lotoflavin.—Before the nature of the pigment, lotoflavin, from *Lotus arabicus* had been elucidated by Wheeler *et al.*,[8] we had considered the possibility that it was the unknown 5 : 7 : 2′ : 4′-tetrahydroxy*iso*flavone. Although this hypothesis was compatible with the available data (for a comprehensive summary see Wheeler *et al.*[8]), the synthesis of this *iso*flavone and several derivatives clearly showed this suggestion to be untenable.

Experimental

Methyl 2 : 4-Dihydroxy-5-methylbenzoate.—(*a*) Prepared in 90% yield by the methylation of 2 : 4-dihydroxy-5-methylbenzoic acid with diazomethane, the *ester* separated from aqueous methanol in stout prisms, m. p. 108° (Found : C, 58·7; H, 5·3; OMe, 17·0. $C_8H_7O_3$·OMe requires C, 59·3; H, 5·5; OMe, 17·0%). (*b*) A solution of 2 : 4-dihydroxy-5-methylbenzoic acid (25 g.) in methanol (150 ml.) containing sulphuric acid (15 ml.) was refluxed for 60 hr., after which most of the methanol was evaporated under reduced pressure and the residue diluted with water (100 ml.). Purification of the crystalline precipitate from aqueous methanol gave the ester (15 g.), identical with that prepared by method (*a*).

[6] Naik, Thakor, and Shah, *Proc. Indian Acad. Sci.*, 1953, **37**, *A*, 765.
[7] Akluwalia, Mukerjee, and Seshadri, *J.*, 1954, 3988.
[8] Doporto, Gallagher, Gowan, Hughes, Philbin, Swain, and Wheeler, *J.*, 1955, 4249.

5 : 4'-*Dihydroxy*-8-*methyl*isoflavone (I; R = R' = H).—Powdered aluminium chloride (10 g.) was added to a solution of methyl 2 : 4-dihydroxy-5-methylbenzoate (4·5 g.) in nitrobenzene (40 ml.) at 5°, followed by a solution of *p*-methoxyphenylacetyl chloride (from 5 g. of acid) in nitrobenzene (25 ml.). The mixture was kept at 30° during 12 days, and after isolation in the usual manner the solid product was repeatedly extracted with methanol and the extracts were concentrated to furnish **2 : 6-*dihydroxy*-4'-*methoxy*-5-*methoxycarbonyl*-3-*methyldeoxybenzoin*** in needles (2·1 g.), m. p. 116°, having an intense red-brown ferric reaction in alcohol [Found : C, 65·0; H, 5·8; OMe, 18·5. $C_{16}H_{12}O_4(OMe)_2$ requires C, 65·4; H, 5·5; OMe, 18·8%].

A solution of this deoxybenzoin (6·5 g.) in alcohol (50 ml.) and water (50 ml.) containing potassium hydroxide (7 g.) was refluxed for 1½ hr. **2 : 6-*Dihydroxy*-4'-*methoxy*-3-*methyldeoxybenzoin*** was obtained which crystallised from methanol in pale yellow prisms (4·5 g.), m. p. 164°, having an intense green ferric reaction in alcohol and insoluble in 2N-sodium hydrogen carbonate, but readily soluble in 2N-sodium hydroxide (Found : C, 70·2; H, 5·9; OMe, 11·4. $C_{15}H_{13}O_3$·OMe requires C, 70·6; H, 5·9; OMe, 11·4%). The mixed m. p. of this ketone with an authentic specimen of 2 : 4-dihydroxy-5-methyl-4'-methoxydeoxybenzoin, m. p. 155°, was about 120°.

Methylation of this ketone (2·8 g.) with dimethyl sulphate (1·5 g., 1·05 ml.) and potassium carbonate in boiling acetone occurred during 1 hr.; a solution of the product in ether was washed with N-sodium hydroxide to remove a trace of alkali-soluble material. Evaporation of the solvent gave 2-hydroxy-6 : 4'-dimethoxy-3-methyldeoxybenzoin as an oil (2·1 g.) having an intense green ferric reaction in alcohol. Cyclisation of this methyl ether (2·1 g.) with ethyl formate (25 ml.) and sodium dust (2 g.) during 24 hr. at 0° furnished an oil which was refluxed in acetic acid (15 ml.) for 5 min. The product, in benzene, was chromatographed on alumina to give **5 : 4'-*dimethoxy*-8-*methyl*isoflavone** which separated from aqueous methanol or benzene–light petroleum (b. p. 60—80°) in needles (1·1 g.), m. p. 137°, devoid of a ferric reaction [Found : C, 72·5; H, 5·4; OMe, 20·1. $C_{16}H_{10}O_2(OMe)_2$ requires C, 73·0; H, 5·4; OMe, 20·9%]. Demethylation of this *iso*flavone (0·4 g.) in boiling hydriodic acid (5 ml., *d* 1·7) and acetic acid (from 2 ml. of anhydride) during 20 min. gave **5 : 4'-*dihydroxy*-8-*methyl*isoflavone**, straw-coloured needles (0·3 g), m. p. 180°, from aqueous acetic acid (Found : C, 71·3; H, 4·4. $C_{16}H_{12}O_4$ requires C, 71·6; H, 4·5%). This *iso*flavone, which has an intense green ferric reaction in alcohol, furnished 5 : 4'-dimethoxy-8-methyl*iso*flavone upon remethylation and gave a *diacetate*, prisms, m. p. 175° (from methanol) (Found : C, 67·8; H, 4·5. $C_{20}H_{16}O_6$ requires C, 68·2; H, 4·6%).

Alkali Degradation of **5 : 4'-*Dimethoxy*-8-*methyl*isoflavone**.—A mixture of 5 : 4'-dimethoxy-8-methyl*iso*flavone (0·4 g.), potassium hydroxide (2 g.), water (2 ml.), and methanol (3 ml.) was heated to 240° and kept thereat for 40 min. The phenolic fraction was isolated in the usual manner from an acidified solution of the cooled reaction mixture in water (25 ml.) and distilled at 160°/0·5 mm., to give 2-hydroxy-4-methoxytoluene (50 mg.), identical with an authentic specimen.

1 : 2-*Di*-(p-*methoxyphenyl*)*ethane*.—The interaction of the Grignard reagent from *p*-methoxybenzyl bromide with 2 : 6-dimethoxybenzonitrile (Robertson [9]) furnished only unchanged nitrile together with the ethane which separated in plates, m. p. 128°, from methanol, identical with an authentic specimen [Found : C, 79·0; H, 7·3; OMe, 25·5. Calc. for $C_{14}H_{12}(OMe)_2$: C, 79·3; H, 7·5; OMe, 25·6%]. Späth [10] records m. p. 126—127°. Demethylation furnished **1 : 2-*di*-(p-*hydroxyphenyl*)*ethane*** in needles, m. p. 198°, from aqueous methanol (Found : C, 77·8; H, 6·5. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·6%).

Methyl **4 : 6-*Dihydroxy*isophthalate**.—4 : 6-Dihydro*iso*phthalic acid (20 g.) was refluxed in methanol (300 ml.) containing sulphuric acid (25 ml.) for 100 hr. The product which separated on cooling was purified from methanol in prisms (17 g.), m. p. 146°. Jois, Manjunath, and Siddappa [11] record m. p. 147° for material prepared by another method.

2 : 4-*Dihydroxy*-4'-*methoxy*-5-*methyldeoxybenzoin* (III; R = Me).—Prepared by the Hoesch condensation of 4-methylresorcinol (5 g.) and 4-methoxybenzyl cyanide (7 g.) in ether (125 ml.) containing zinc chloride (4 g.) during 3 days, 2 : 4-dihydroxy-4'-methoxy-5-methyldeoxybenzoin (4 g.) separated from light petroleum (b. p. 60—80°) in prisms, m. p. 154°, having an

[9] Robertson, *J.*, 1933, 1163.
[10] Späth, *Monatsh.*, 1913, **34**, 1999.
[11] Jois, Manjunath, and Siddappa, *Half-yearly J., Mysore Univ.*, 1932, **6**, 96; *Chem. Abs.*, 1933, **27**, 5069.

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intense red-brown ferric reaction in alcohol (Found: C, 70·4; H, 5·9. Calc. for $C_{16}H_{16}O_4$: C, 70·6; H, 5·9%). Bhandari, Bose, and Siddiqui [5] record m. p. 139—140°.

5-Carboxy-2:4-dihydroxy-4′-methoxydeoxybenzoin (III; R = CO_2H).—A solution of *p*-methoxyphenylacetyl chloride (10 g.) in nitrobenzene (25 ml.) was added at 0° to nitrobenzene (80 ml.) containing aluminium chloride (20 g.) and methyl 2:4-dihydroxybenzoate (12 g.). After 48 hr. the product was isolated and the nitrobenzene recovered by steam-distillation. A solution of the semicrystalline residue in 4N-potassium hydroxide (400 ml.) was refluxed for ½ hr., to give *5-carboxy-2:4-dihydroxy-4′-methoxydeoxybenzoin* (8·5 g.) which separated from aqueous methanol in prisms, m. p. 200°, having an intense blood-red ferric reaction in alcohol (Found: C, 63·5; H, 5·1; OMe, 9·5. $C_{15}H_{11}O_5$·OMe requires C, 63·6; H, 4·7; OMe, 10·2%). This ketone was soluble in 2N-sodium hydrogen carbonate and was unaffected by boiling 20% (w/v) aqueous potassium hydroxide solution during 1½ hr.

Methylation by the dimethyl sulphate–potassium carbonate method in boiling acetone during 4 hr. gave, quantitatively, 2:4:4′-*trimethoxy-5-methoxycarbonyldeoxybenzoin* which formed plates, m. p. 157°, from methanol and had no ferric reaction in alcohol [Found: C, 65·7; H, 5·8; OMe, 36·0. $C_{15}H_8O_2(OMe)_4$ requires C, 66·3; H, 5·8; OMe, 36·0%].

Decarboxylation of 5-carboxy-2:4-dihydroxy-4′-methoxydeoxybenzoin (2 g.) in boiling quinoline (15 ml.) containing copper bronze (0·5 g.) was effected during 5 min. (longer reaction caused extensive decomposition). The product crystallised from benzene and then from aqueous methanol in needles (0·45 g.), m. p. 158°, identical with an authentic specimen of 2:4-dihydroxy-4′-methoxydeoxybenzoin.

5:4′-Dimethoxy-8-methyl-7-toluene-p-*sulphonyloxy*isoflavone (I; R′ = toluene-*p*-sulphonyloxy, R = Me).—Interaction of 2:4-dihydroxy-6:4′-dimethoxy-3-methyldeoxybenzoin [3] (8 g.), benzyl bromide (5·0 g., 1·1 mol.), and potassium carbonate (20 g.) in boiling acetone (250 ml.) during 3 hr., gave *4-benzyloxy-2-hydroxy-6:4′-dimethoxy-3-methyldeoxybenzoin* (8 g.) which separated from methanol in needles, m. p. 118°, with an intense violet ferric reaction in alcohol (Found: C, 73·2; H, 6·5. $C_{24}H_{24}O_5$ requires C, 73·5; H, 6·2%).

Cyclisation of this ketone (7·5 g.) with sodium dust (3 g.) and ethyl formate (50 ml.) furnished *7-benzyloxy-2-hydroxy-5:4′-dimethoxy-8-methyl*isoflavanone (6·5 g.), prisms, m. p. 127° (decomp.), from methanol, devoid of a ferric reaction (Found: C, 68·7; H, 5·9. $C_{25}H_{24}O_6.H_2O$ requires C, 68·5; H, 6·0%). When boiled for 5 min. in acetic acid it was converted quantitatively into *7-benzyloxy-5:4′-dimethoxy-8-methyl*isoflavone which formed needles, m. p. 168°, from methanol (Found: C, 74·1; H, 5·2. $C_{25}H_{22}O_5$ requires C, 74·6; H, 5·5%). Catalytic debenzylation of this *iso*flavone (3 g.) in acetic acid (100 ml.) with a catalyst prepared from charcoal (1 g.), palladium chloride (0·4 g.), and hydrochloric acid (5 ml.) for 1 hr. gave quantitatively 7-hydroxy-5:4′-dimethoxy-8-methyl*iso*flavone identical with that prepared by another method.[2] The *toluene*-p-*sulphonate*, prepared quantitatively in pyridine at room temperature during 48 hr., separated from acetone in prisms, m. p. 212° [Found: C, 64·8; H, 5·4; OMe, 13·7. $C_{25}H_{22}O_7S(OMe)_2$ requires C, 64·4; H, 4·7; OMe, 13·3%].

Of numerous attempts to remove the toluene-*p*-sulphonyl group by reduction from this *iso*flavone, the following experiment is typical. A rapid stream of hydrogen was passed through a solution of the toluene-*p*-sulphonate (1 g.) in methanol (2 l.) containing Raney nickel (5 g.) for 1 hr. and the concentrated solution was then fractionally crystallised to yield: (*a*) unchanged material (0·1—0·2 g.); (*b*) *7-hydroxy-5:4′-dimethoxy-8-methyl*isoflavanone (0·1 g.), needles, m. p. 260°, from ethanol, devoid of a ferric reaction and readily soluble in cold 2N-sodium hydroxide [Found: C, 68·0; H, 5·8; OMe, 20·2. $C_{16}H_{12}O_3(OMe)_2$ requires C, 68·7; H, 5·7; OMe, 19·7%] (the mixed m. p. with the corresponding *iso*flavone was *ca.* 245°); and (*c*) *5:4′-dimethoxy-8-methyl-7-toluene*-p-*sulphonyloxy*isoflavanone (0·1 g.), needles, m. p. 149°, from ethanol devoid of a ferric reaction and insoluble in 2N-sodium hydroxide [Found: C, 63·8; 64·1; H, 5·1, 5·0; OMe, 13·3. $C_{23}H_{20}O_5S(OMe)_2$ requires C, 64·4; H, 4·7; OMe, 13·3%].

4-Methylresorcinol (With J. Staunton).—The following process is a substantial improvement upon those previously described. A solution of 2:4-dihydroxybenzaldehyde (40 g.) in water (200 ml.) and concentrated hydrochloric acid (200 ml.) containing zinc amalgam (200 g.) was stirred vigorously for 2 hr., with the addition of further hydrochloric acid (50 ml.) after 1 hr. Next day the decanted solution was saturated with ammonium sulphate and exhaustively extracted with ether, and the extract distilled to give 4-methylresorcinol (19—20 g.), m. p. 99—100°.

5 : 7 : 2′ : 4′-*Tetrahydroxy*isoflavone.—A solution of 5 : 7 : 2′ : 4′-tetramethoxy*iso*flavone [12] (3·7 g.) in benzene (100 ml.) containing aluminium chloride (10 g.) was heated on the steam-bath for 4 hr. The product was purified from aqueous methanol or aqueous acetic acid, to furnish 5 : 7 : 2′ : 4′-*tetrahydroxy*isoflavone (2·5 g.) in pale yellow needles, m. p. 272°, having an intense red violet-brown ferric reaction in alcohol (Found : C, 62·7; H, 3·8. $C_{15}H_{10}O_6$ requires C, 62·9; H, 3·5%).

Methylation with dimethyl sulphate–potassium carbonate in boiling acetone for ½ hr. furnished an almost quantitative yield of 5-*hydroxy*-7 : 2′ : 4′-*trimethoxy*isoflavone which separated from methanol in needles, m. p. 154°, with an intense red-brown ferric reaction [Found : C, 65·1; H, 5·2; OMe, 27·7. $C_{15}H_7O_3(OMe)_3$ requires C, 65·8; H, 4·9; OMe, 28·4%]. 5-*Acetoxy*-7 : 2′ : 4′-*trimethoxy*isoflavone separated from methanol in plates, m. p. 204°, devoid of a ferric reaction (Found : C, 64·6; H, 5·3. $C_{20}H_{18}O_7$ requires C, 64·9; H, 4·9%).

The 4-methylresorcinol was prepared by Mr. K. Turner, B.Sc., and the analyses were performed by Mr. A. S. Inglis, M.Sc., and his associates of this Department.

UNIVERSITY OF LIVERPOOL. [*Received, November 15th*, 1956.]

[12] Whalley, *J.*, 1953, 3366; King and Neil, *J.*, 1952, 4752.

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346. *The Synthesis of Polycyclic Aromatic Hydrocarbons. Part I. A Synthesis of Optically Active* 9 : 10-*Dihydrodinaphtho*(2′ : 3′-3 : 4)-(2″ : 3″-5 : 6)*phenanthrene, and a New Synthesis of Pentaphene.*

By G. M. BADGER, P. R. JEFFERIES, and R. W. L. KIMBER.

The "intramolecularly overcrowded" 9 : 10-dihydrodinaphthophenanthrene (III) has been prepared by cyclisation of 2 : 2′-bisbromomethyl-1 : 1′-dianthryl (II; R = Br) with phenyl-lithium, and its (+)- and (−)-forms have been similarly prepared from the (+)- and the (−)-form of the bisbromomethyl-compound. The optically active forms of the hydrocarbon have $[\alpha]_D^{16}$ *ca.* 2000° in benzene and a half-life in boiling xylene of 27 minutes. Dehydrogenation could not be effected without racemisation.

Pentaphene (XI) has likewise been synthesised by cyclisation of 3 : 3′-bisbromomethyl-2 : 2′-dinaphthyl (VIII; R = Br), followed by dehydrogenation.

HALL and TURNER'S elegant method [1] for the preparation of 9 : 10-dihydrophenanthrene by the action of phenyl-lithium on 2 : 2′-bisbromomethyldiphenyl promises to be of increasing value for the synthesis of more complex polycyclic hydrocarbons. It has already been applied in syntheses of substituted phenanthrenes,[2] 3 : 4-benzophenanthrene,[3] picene,[4] 3 : 4-5 : 6-dibenzophenanthrene,[5] and optically active 9 : 10-dihydro-3 : 4-5 : 6-dibenzophenanthrene.[6] As part of a study of "intramolecular overcrowding" [7] in polycyclic compounds, this method has now been used to prepare 9 : 10-dihydrodinaphtho(2′ : 3′-3 : 4)(2″ : 3″-5 : 6)phenanthrene (III). This molecule is much crowded, and by analogy with related compounds must be considerably distorted from a planar structure, so was expected to exist in highly optically active forms (cf. ref. 6). This has been confirmed. Hall and Turner's method [1] has also been used in a synthesis of pentaphene (XI) from 3 : 3′-bisbromomethyl-2 : 2′-dinaphthyl (VIII; R = Br).

1 : 1′-Dianthryl-2 : 2′-dicarboxylic acid [8] with diazomethane gave the methyl ester (I) which was reduced with lithium aluminium hydride to a diol (II; R = OH) [characterised

[1] Hall and Turner, *Nature*, 1949, **163**, 537; Hall, Lesslie, and Turner, *J.*, 1950, 711.
[2] Hall and Turner, *J.*, 1951, 3072; Bergmann and Pelchowicz, *J. Amer. Chem. Soc.*, 1953, **75**, 2663; Bergmann and Pelchowicz, *J. Org. Chem.*, 1954, **19**, 1387; Wittig and Zimmermann, *Chem. Ber.*, 1953, **86**, 629.
[3] Bergmann and Pelchowicz, *J. Org. Chem.*, 1954, **19**, 1383.
[4] Jefferies, *Chem. and Ind.*, 1955, 1425.
[5] Bergmann and Szmuszkovicz, *J. Amer. Chem. Soc.*, 1951, **73**, 5153.
[6] Hall and Turner, *J.*, 1955, 1242.
[7] Harnik, Herbstein, Schmidt, and Hirshfeld, *J.*, 1954, 3288.
[8] Bell and Waring, *J.*, 1949, 1579.

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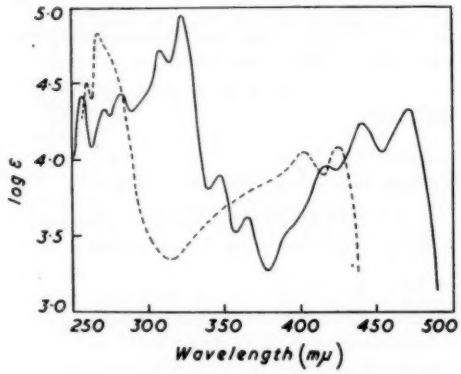
as the acetyl derivative (II; R = OAc)]; this was converted into 2 : 2′-bisbromomethyl-1 : 1′-dianthryl (II; R = Br) with hydrobromic acid in acetic acid, whence phenyllithium in benzene gave the dihydrodinaphthophenanthrene (III) in satisfactory overall yield.

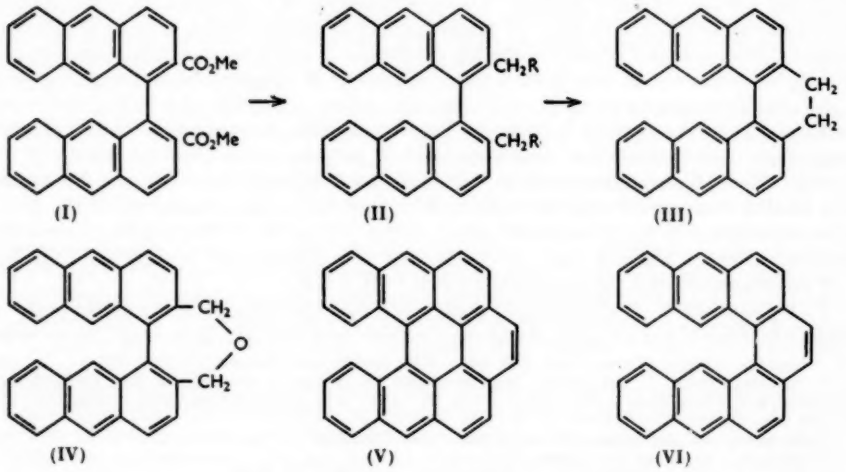
(+)- and (−)-1 : 1′-Dianthryl-2 : 2′-dicarboxylic acid are readily available [8] and were similarly used. To avoid racemisation, somewhat milder conditions were used for preparation of the bromides, and a small amount of (probably) the cyclic ether (IV) was isolated along with the (−)-dibromide. The (−)-dibromide gave a hydrocarbon (III) having $[\alpha]_D^{16}$ −2007° ± 10° in benzene, and the (+)-dibromide gave a hydrocarbon with $[\alpha]_D^{16}$ +1980° ± 40°. This very large specific rotation may be compared with that (1500°)



Absorption spectra in dioxan of dinaphtho-(2′ : 3′-3 : 4)(2″ : 3″-5 : 6)phenanthrene (?) (———) and its 9 : 10-dihydro-derivative (– – – –).

for optically active 9 : 10-dihydro-3 : 4-5 : 6-dibenzophenanthrene.[6] The (−)-form was unchanged after 6 hours in refluxing benzene; but in boiling xylene had a half-life of 27 ± 1 min. (rate constant 2·6 ± 0·1 × 10^{-2} min.$^{-1}$).

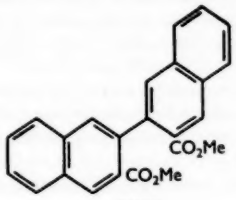
Dehydrogenation of the (±)-hydrocarbon with palladium–charcoal in boiling *p*-cymene gave smoothly an aromatic hydrocarbon which, from its absorption spectrum (see Figure)



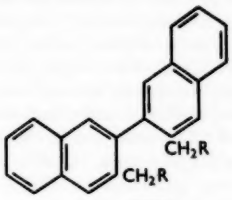
and other properties, appears to be the expected dinaphthophenanthrene (VI), though the evidence does not exclude its being 1 : 12-5 : 6-7 : 8-tribenzoperylene (V). The latter

hydrocarbon is unknown, although Clar [9] has given some data for the light absorption of a mixture of *meso*-anthrodianthrene and of a hydrocarbon believed to have this structure.

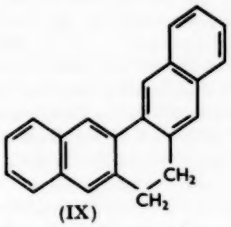
Attempts to dehydrogenate either the racemate or the (−)-form under milder conditions with *N*-bromosuccinimide failed.



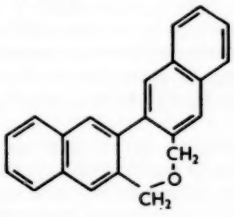
(VII)



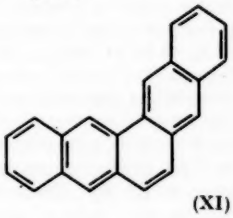
(VIII)



(IX)



(X)



(XI)

For the synthesis of pentaphene (XI), methyl 2 : 2′-dinaphthyl-3 : 3′-dicarboxylate (VII) was reduced with lithium aluminium hydride, and the resulting diol (VIII; R = OH) converted into the bisbromomethyl. compound (VIII; R = Br). Some difficulty was experienced in the cyclisation of this product with phenyl-lithium and satisfactory yields were never obtained. Under the most favourable conditions the crude 6 : 7-dihydropentaphene (IX) was contaminated with insoluble material and the cyclic ether (X). The last compound was also prepared by dehydration of the diol (VIII; R = OH), in diphenyl ether, with anhydrous hydrogen chloride.

Dehydrogenation of dihydropentaphene with palladium–charcoal in boiling *p*-cymene gave pentaphene (XI), identical with that described by Clar *et al.*[10] Although the present synthesis gives no higher yield than the earlier methods it is unambiguous.

Experimental

Dimethyl 1 : 1′-*Dianthryl*-2 : 2′-*dicarboxylate*.—(i) A solution of (±)-1 : 1′-dianthryl-2 : 2′-dicarboxylic acid [8] (4 g.) in dioxan (40 c.c.) was treated with diazomethane (2·5 mols.) in ether at room temperature. After 10 min., the ether was evaporated and water (20 c.c.) added. Recrystallisation from ethanol gave the *ester* (4·25 g., 100%) as pale yellow needles, m. p. 238—239° (Found: C, 81·6; H, 5·0. $C_{32}H_{22}O_4$ requires C, 81·7; H, 4·7%).

(+)-*Methyl* 1 : 1′-*dianthryl*-2 : 2′-*dicarboxylate*. After recrystallisation the (+)-*ester* had m. p. 228—230°, $[\alpha]_D^{15}$ +382° (*c* 0·335 in acetone) (Found: C, 81·6; H, 4·7%), and the (−)-*ester*, m. p. 228—230°, $[\alpha]_D^{15}$ −387° (*c* 0·450 in acetone) (Found: C, 82·0; H, 5·0%).

2 : 2′-*Bisbromomethyl*-1 : 1′-*dianthryl*.—(i) The (±)-methyl ester (4 g.) in ether (400 c.c.) was refluxed with lithium aluminium hydride (5·2 g.) in ether (400 c.c.) for 6 hr. The crude diol (3·3 g., 95%) could not be obtained constant-melting (dehydration during recrystallisation?) and satisfactory analyses were not obtained. (±)-2 : 2′-*Bisacetoxymethyl*-1 : 1′-*dianthryl*, prepared in pyridine with acetic anhydride, formed pale yellow needles, m. p. 232—233°, from light petroleum (b. p. 100—120°), (Found: C, 81·7; H, 5·3. $C_{36}H_{28}O_4$ requires C, 81·9; H, 5·2%).

The crude diol (1 g.) in boiling glacial acetic acid (25 c.c.) was treated with hydrobromic acid in glacial acetic acid (7·5 c.c.; 50% w/v). After 15 min. a further quantity (5 c.c.) of

[9] Clar, *Chem. Ber.*, 1949, **82**, 54.
[10] Clar and John, *Ber.*, 1931, **64**, 981; 1930, **63**, 2975; Clar and Stewart, *J.*, 1951, 3215.

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hydrobromic acid was added, and heating continued for ½ hr. The product (1·2 g.) was chromatographed in benzene on alumina and recrystallised from ethyl methyl ketone. (±)-**2 : 2′-*Bisbromomethyl*-1 : 1′-*dianthryl*** was obtained as yellow-orange prisms, m. p. 217—219° (Found : C, 66·9; H, 4·0. $C_{30}H_{20}Br_2$ requires C, 66·7; H, 3·7%).

(ii) Reduction of the (+)-methyl ester in the same way gave a crude diol, $[\alpha]_D^{15}$ +460°, characterised as the (+)-**2 : 2′-*bisacetoxymethyl*-1 : 1′-*dianthryl***. After recrystallisation from light petroleum (b. p. 100—120°) it formed pale yellow prisms, m. p. 180—181°, $[\alpha]_D^{15}$ +290° (*c* 0·266 in acetone) (Found : C, 81·8; H, 5·4. $C_{34}H_{26}O_4$ requires C, 81·9; H, 5·2%).

Conversion into the bromo-compound was effected as for the racemate except that the whole of the hydrobromic acid was added at once and the total time of refluxing was only 5 min. (+)-**2 : 2′-*Bisbromomethyl*-1 : 1′-*dianthryl*** was obtained as yellow-orange prisms, m. p. 224—226°, $[\alpha]_D^{15}$ +195° (*c* 0·230 in C_6H_6) (Found : C, 67·1; H, 3·9%).

(iii) Similarly the (−)-methyl ester gave a crude diol, $[\alpha]_D^{15}$ −471°, which was characterised as the (−)-**2 : 2′-*bisacetoxymethyl*-1 : 1′-*dianthryl***, pale yellow needles (from light petroleum), m. p. 180—181°, $[\alpha]_D^{15}$ −290° (*c* 0·248 in acetone) (Found : C, 81·6; H, 5·4%). (−)-**2 : 2′-*Bisbromomethyl*-1 : 1′-*dianthryl*** was obtained as yellow orange prisms, m. p. 224—226°, $[\alpha]_D^{15}$ −188° (*c* 0·392 in C_6H_6) (Found : C, 66·8; H, 4·2%). Further elution of the column gave ***dianthro*-(2′ : 1′-3 : 4)(1″ : 2″-5 : 6)*oxepin*** (IV) which crystallised from benzene in yellow prisms, m. p. 272—275°, $[\alpha]_D^{16}$ −1530° (*c* 0·354 in C_6H_6) (Found : C, 90·6; H, 5·3; O, 4·2. $C_{30}H_{20}O$ requires C, 90·9; H, 5·1; O, 4·0%).

9 : 10-*Dihydrodinaphtho*(2′ : 3′-3 : 4)(2″ : 3″-5 : 6)*phenanthrene*.—(i) A solution of phenyl-lithium (4·6 c.c., 1·2 mols.; see below) in anhydrous benzene was added in portions, during 15 min., to a shaken solution of the (±)-dibromide (2·2 g.) in anhydrous benzene (20 c.c.) in nitrogen. After being shaken for further 15 min. the mixture was refluxed for ½ hr. Decomposition with water and hydrochloric acid, and recrystallisation of the product from benzene, gave the ***dihydro*-compound** (1·1 g., 75%) as yellow needles, m. p. 303—305° (Found : C, 94·4; H, 5·3. $C_{30}H_{20}$ requires C, 94·7; H, 5·3%). Its benzene solution had a bright blue fluorescence. Light absorption in dioxan : $\lambda_{max.}$ 267, 259, 402, and 424 mμ (log ε 4·84, 4·51, 4·06, 4·10).

(ii) In the same way the (+)-dibromide was converted into the (+)-***compound***, yellow needles (from benzene), m. p. 295—297°, $[\alpha]_D^{16}$ +1980° ± 40° (*c* 0·072 in C_6H_6) (Found : C, 94·9; H, 5·4%); the (−)-***analogue*** had m. p. 295—297°, $[\alpha]_D^{15}$ −2007° ± 10° (*c* 0·142 in C_6H_6) (Found : C, 94·7; H, 5·45%).

(?)-*Dinaphtho*(2′ : 3′-3 : 4)(2″ : 3″-5 : 6)*phenanthrene*.—A mixture of the (±)-dihydrodinaphthophenanthrene (0·5 g.), 10% palladium–charcoal (0·4 g.), and *p*-cymene (30 c.c.) was heated under reflux for 4 hr. Removal of the solvent *in vacuo* from the filtered solution and recrystallisation from benzene gave the crude product (0·4 g.), m. p. 290°, which was chromatographed from benzene on alumina and recrystallised from benzene. The ***product*** was orange needles, m. p. 293—295° (Found : C, 95·3; H, 4·5. $C_{30}H_{18}$ requires C, 95·2; H, 4·8%). Light absorption in dioxan : $\lambda_{max.}$ 257, 272, 282, 308, 322, 348, 365, 418, 440, and 472 mμ (log ε 4·43, 4·35, 4·28, 4·71, 4·96, 3·90, 3·62, 3·95, 4·24, 4·33).

3 : 3′-*Bishydroxymethyl*-2 : 2′-*dinaphthyl*.—A suspension of methyl 2 : 2′-dinaphthyl-3 : 3′-dicarboxylate [11] (10 g.) in boiling anhydrous ether (500 c.c.) was added to a boiling suspension of lithium aluminium hydride (13 g.) in ether (500 c.c.), and the mixture refluxed for 2 hr. Decomposition with water and dilute sulphuric acid gave **3 : 3′-*bishydroxymethyl*-2 : 2′-*dinaphthyl*** (7·7 g., 92%), needles (from ethanol), m. p. 228—229° (Found : C, 83·7; H, 6·0. $C_{22}H_{18}O_2$ requires C, 84·1; H, 5·8%). **3 : 3′-*Bisacetoxymethyl*-2 : 2′-*dinaphthyl***, formed in pyridine with acetic anhydride, crystallised from ethanol in pale yellow needles, m. p. 106—106·5° (Found : C, 78·5; H, 5·8. $C_{26}H_{22}O_4$ requires C, 78·4; H, 5·5%).

3 : 3′-*Bisbromomethyl*-2 : 2′-*dinaphthyl*.—Hydrobromic acid in glacial acetic acid (15 c.c.; 50% w/v) was added to a boiling solution of the above diol (2 g.) in glacial acetic acid. After 15 minutes' refluxing a further 10 c.c. of hydrobromic acid were added and heating maintained for a further ½ hr. **3 : 3′-*Bisbromomethyl*-2 : 2′-*dinaphthyl*** (2·6 g., 93%) separated on cooling; it crystallised from ethyl methyl ketone in needles, m. p. 165—166° (Found : C, 60·0; H, 3·5. $C_{22}H_{16}Br_2$ requires C, 60·0; H, 3·6%).

6 : 7-*Dihydropentaphene*.—A stock solution of phenyl-lithium was prepared from bromobenzene (22 g.) lithium (3 g.), and ether (80 c.c.), and made up to 100 c.c. with ether.

[11] Martin, *J.*, 1941, 679.

Phenyl-lithium solution (8·4 c.c.; 2·2 mols.) was added in portions during 15 min. to 3 : 3′-bisbromomethyl-2 : 2′-dinaphthyl (2·0 g.) in benzene (20 c.c.). After refluxing for ½ hr. the mixture was decomposed with water and dilute hydrochloric acid and filtered. The organic layer was dried and chromatographed on alumina (15 × 3 cm.). Elution with benzene–hexane (1 : 4; 250 c.c.) and recrystallisation from benzene gave 6 : 7-*dihydropentaphene* (0·36 g., 30%) as needles, m. p. 140—141° (Found: C, 94·0; H, 5·7. $C_{22}H_{16}$ requires C, 94·3; H, 5·7%). Light absorption in $CHCl_3$: $\lambda_{max.}$ 264, 279, and 321 mμ (log ε 4·45, 4·34, 4·19).

Further elution of the column with benzene–hexane (1 : 1; 250 c.c.) and recrystallisation of the product (50 mg.) from benzene–hexane (1 : 1) gave *dinaphtho*(2′ : 3′-3 : 4)(2″ : 3″-5 : 6)-*oxepine* (X) as prisms, m. p. 223—224° (Found: C, 89·0; H, 5·6; O, 5·9. $C_{22}H_{16}O$ requires C, 89·2; H, 5·4; O, 5·4%). The m. p. was not depressed by admixture with a specimen prepared by passing dry hydrogen chloride into a solution of 3 : 3′-bishydroxymethyl-2 : 2′-dinaphthyl (0·5 g.) in diphenyl ether (10 c.c.) at 100°.

Pentaphene.—A mixture of 6 : 7-dihydropentaphene (0·3 g.), 10% palladium–charcoal (0·2 g.), and *p*-cymene (20 c.c.) was refluxed for 4 hr. Evaporation of the filtrate *in vacuo* and recrystallisation of the product from glacial acetic acid and from ethanol gave pentaphene (0·2 g., 67%) as pale greenish-yellow needles, m. p. 255—257° in agreement with the literature (Found: C, 94·6; H, 5·0. Calc. for $C_{22}H_{14}$: C, 94·9; H, 5·0%). The absorption curve was identical with that given by Clar,[10] and the dipicrate had m. p. 184° (lit., m. p. 184°). Oxidation with osmium tetroxide by Cook and Schoental's method [12] gave an unstable diol which was further oxidised with sodium dichromate to *pentaphene*-6 : 7-*quinone*, red plates, m. p. 326—328° (vac.) (Found: C, 85·3; H, 4·1. $C_{22}H_{12}O_2$ requires C, 85·7; H, 3·9%). Light absorption in $CHCl_3$: $\lambda_{max.}$ 253, 267, 283, 292, 304, 326, 378, 468, and 488 mμ (log ε 4·61, 4·49, 4·49, 4·46, 4·26, 4·45, 3·85, 3·41, 3·39).

Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne. We also thank E. I. du Pont de Nemours and Co. for a gift of dimethyldianthraquinonyl, which was used to prepare dianthryldicarboxylic acid.

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, November 11th,* 1956.]

[12] Cook and Schoental, *J.*, 1948, 170.

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347. *The Kinetics of the Reduction of Thallium*(III) *by the Trisdipyridylosmium*(II) *Ion in Aqueous Perchloric Acid.*

By D. H. IRVINE.

The rate of the reaction between thallium(III) and trisdipyridylosmium(II) ion, unlike that between thallium(III) and ferrous ion, increases slightly as the hydrogen-ion concentration is increased. The data can be interpreted by assuming that both unhydrolysed Tl^{3+}, as well as $Tl(OH)^{2+}$, react with $Os(dipy)_3^{2+}$. The values of the respective constants for the two reactions are $3{\cdot}6 \times 10^6 \exp(-6900 \pm 800/RT)$ l. mole^{-1} sec.$^{-1}$ and $3{\cdot}6 \times 10^9 \exp(-11{,}500 \pm 1000/RT)$ l. mole^{-1} sec.$^{-1}$. Chloride ions show the same retardation of the rate as in the analogous reaction of ferrous ions.

THE kinetics of the reduction of thallium(III) by simple aquated ferrous ion [1,2,3] is slow, the second-order constant at 25° being of the order of 10^{-2} l. mole^{-1} sec.$^{-1}$, and the rate increases as the hydrogen-ion concentration is decreased. Johnson [1] interpreted the results of the hydrogen-ion dependence on the basis that simple ferrous ion reacted with the hydrolysed species of Tl^{3+}, *viz.*, $Tl(OH)^{2+}$ and TlO^+, but Ashurst and Higginson [3] pointed out that there is no way of distinguishing from the data between such a mechanism and one in which unhydrolysed Tl^{3+} reacts with the hydrolysed species of ferrous ion.

[1] Johnson, *J. Amer. Chem. Soc.*, 1952, **74**, 959.
[2] Forchheimer and Epple, *ibid.*, p. 5772.
[3] Ashurst and Higginson, *J.*, 1953, 3044.

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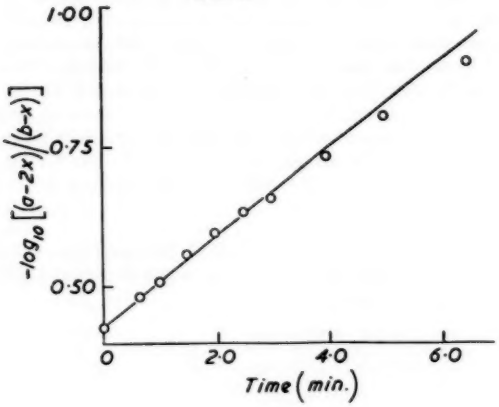
In an attempt to find out whether the reduction of thallium(III) by a complex ion presented any essentially different features from its reduction by a simple aquated ion, the reaction between thallium(III) and $Os(dipy)_3^{2+}$ was investigated. Earlier work by George and Irvine [4] on the reduction of thallic ion by the ferrous tris-*o*-phenanthroline ion had suggested a close parallel between this reaction and that between thallium(III) and ferrous ion. However, a further investigation (unpublished results) of the former reaction indicated that the results were not significant as they corresponded to the irreversible oxidation of the ferrous tris-*o*-phenanthroline ion.

The reduction of thallium(III) by $Os(dipy)_3^{2+}$ is reversible in the sense that all the original $Os(dipy)_3^{2+}$ can be recovered after the reaction by addition of a reducing agent. As in the case of the analogous reaction with ferrous ion a departure from second-order

FIG. 1.



kinetics was observed after about 60—70% of reaction. This can be seen in Fig. 1 which shows an example of the simple second-order plot [a = initial concentration of $Os(dipy)_3^{2+}$, b = initial concentration of thallium(III), and x is the amount by which thallium(III) is reduced in time t]. Ashurst and Higginson [3] attribute the departure from second-order kinetics, in the case of the ferrous ion reaction, to the retarding effect of iron(III) formed during the reaction, and presumably a similar explanation is applicable here. In other words, the overall reaction probably involves the following steps:

$$Tl^{III} + Os(dipy)_3^{2+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Tl^{II} + Os(dipy)_3^{3+} \quad . \quad . \quad . \quad . \quad (1)$$

$$Tl^{II} + Os(dipy)_3^{2+} \xrightarrow{k_2} Tl^{I} + Os(dipy)_3^{3+} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Dependence of the Rate of the Reaction on the Hydrogen-ion Concentration.—The rate of the reaction between thallium(III) and $Os(dipy)_3^{2+}$ increased slightly as the hydrogen-ion concentration was increased. This behaviour is in contrast with the analogous reaction with ferrous ion where the rate decreased substantially with increased concentration of hydrogen ions. Table 1 shows the results of experiments carried out at 24·5°, with corresponding values for the reaction of ferrous ion for comparison. The values of the observed velocity constants (k_1) in this Table were derived from the slopes of the simple second-order plots. It is clear from Ashurst and Higginson's [3] work that values of k_1 obtained in this way are accurate.

[4] George and Irvine, *J.*, 1954, 587.

The data in Table 1 can be explained by assuming that $Os(dipy)_3^{2+}$ reacts with both unhydrolysed Tl^{3+} and $Tl(OH)^{2+}$. On this interpretation the observed velocity constant (k_1) of the reaction is given by the equation

$$k_1 = (k_a[H^+] + k_bK)/(K + [H^+]) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where k_a and k_b are the velocity constants for the reaction between $Os(dipy)_3^{2+}$ and Tl^{3+} and $Tl(OH)^{2+}$ respectively, and K is the first hydrolysis constant of thallic ion. A plot of $k_1(K + [H^+])$ against $[H^+]$ from results in Table 1 is shown in Fig. 2. A value of

TABLE 1. *Effect of the hydrogen-ion concentration on the rate of the reaction between* Tl^{III} *and* $Os(dipy)_3^{2+}$.

$[H^+]$	2·99	1·92	0·98	0·52
k_1 (l. mole^{-1} sec.$^{-1}$).....	21·7	19·4	17·3	16·6
$10^2k_1'$ (l. mole^{-1} sec.$^{-1}$) for ferrous ion reaction	1·20	1·50	2·20	3·33

Ionic strength = 2·99; Temp. = 24·5°.
The results in row 3 were interpolated from ref. 1.

$K(= 6{\cdot}4)$ at this temperature was obtained by interpolation from Johnson's [1] results. The plot is linear and shows that a mechanism in which both Tl^{3+} and $Tl(OH)^{2+}$ react with $Os(dipy)_3^{2+}$ is consistent with the observations.

A similar expression to eqn. (3) can be obtained by assuming that the unhydrolysed Tl^{3+} reacts with $Os(dipy)_3^{2+}$ as well as a conjugate acid species $Os(dipy)_3H^{3+}$. On this basis the velocity constant of the reaction can be expressed by the equation

$$k^1 = \frac{[H^+]}{K + [H]}\left(\frac{k_a'[H^+]}{K_D + [H^+]} + \frac{k_b'K_D}{K_D + [H^+]}\right) \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where k_a' and k_b' are the velocity constants for the reaction of Tl^{3+} with $Os(dipy)_3H^{3+}$ and $Os(dipy)_3^{2+}$ respectively and K_D is the dissociation constant of the acid $Os(dipy)_3H^{3+}$.

If $K_D \ll [H^+]$ then eqn. (4) reduces to

$$K_1 = (k_a'[H^+] + k_b'K_D)/(K + [H^+]) \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

which is of the same form as eqn. (3). A decision as to whether equation (3) or equation (4) is a truer representation of the dependence of the rate on the hydrogen-ion concentration could be made by working at low hydrogen-ion concentration. Unfortunately this was not possible because of hydrolysis of thallic ion below a concentration of hydrogen ion of 0·3M. However, E.M.F. measurements on the $Os(dipy)_3^{2+}$–$Os(dipy)_3^{3+}$ couple [5] give no support for the assumption that K_D is much smaller than $[H^+]$ since the E.M.F. of the couple is unaffected by a change of hydrogen-ion concentration in the range 0·001M—0·025M. Accordingly eqn. (3) is preferred.

The Effect of Temperature on the Rate.—The rate of the reaction was measured at 17·5°, 24·5°, and 35·0° at various hydrogen-ion concentrations. A linear plot of $k_1(K + [H^+])$ against $[H^+]$ was obtained at each temperature and from these plots values of k_a and k_bK were obtained. Values of K of 5·1, 6·4, and 9·1 at these temperatures respectively were interpolated from Johnson's results,[1] and thence the corresponding values of k_b were determined. The values of k_a and k_b are recorded in Table 2. Expressed according to the Arrhenius equation, the values of k_a and k_b are $3{\cdot}6 \times 10^6 \exp(-6900 \pm 800/RT)$ and $3{\cdot}6 \times 10^9 \exp(-11{,}500 \pm 1000/RT)$ l. mole^{-1} sec.$^{-1}$ respectively. It is noteworthy that the ratio of 10^3 between the A factors is comparable with

[5] Barnes, Dwyer, and Gyarfas, *Trans. Faraday Soc.*, 1952, **48**, 269.

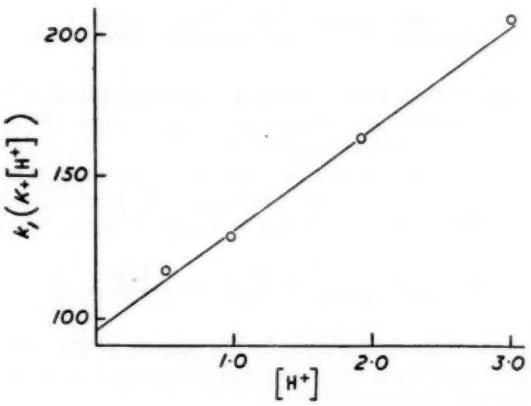
that of 10^4 predicted by Glasstone, Laidler, and Eyring [6] for the reactions between $M_a^{2+} + M_b^{3+}$ and $M_a^{2+} + M_{b'}^{2+}$. The activation energies for the processes are smaller than those for the thallous–thallic exchange [7] and for the reduction of thallium(III) by ferrous ion.

TABLE 2. *Effect of temperature on the rate of the reaction* (*ionic strength* = 2·99).

Temp.	k_a (l. mole^{-1} sec.$^{-1}$)	k_b (l. mole^{-1} sec.$^{-1}$)
17·5°	29·0 ± 2·0	8·4 ± 0·3
24·5	36·0 ± 2·0	14·7 ± 0·3
35·0	53·0 ± 6·0	23·5 ± 0·6

In terms of Zwolinski, Marcus, and Eyring's [8] picture of electron-transfer processes this is presumably due to the smaller degree of reorganisation required by the complex ion in the transition state. The difference in activation energies for the two processes is, however,

FIG. 2.



difficult to understand. Different transfer processes seem to be indicated, though having the osmium(II) in the form of a complex ion presumably rules out the possibility of hydrogen-atom transfer. More data on the reactions of complex ions in solution are highly desirable in order to explain this and other phenomena. There is, for instance, George and Irvine's observation [4] that reactions between complex ions of like charge can proceed with velocity constants greater than 10^5 l. mole^{-1} sec.$^{-1}$.

TABLE 3. *Effect of chloride ion on the rate of reaction.*

$10^5[Cl^-]$	9	4·0	7·0	10·0	100·0
k_1 (l. mole^{-1} sec.$^{-1}$)	19·3	6·6	2·9	1·7	very slow

Ionic strength = 2·99; $[H^+]$ = 0·98M; temp. = 27·0°.

The Effect of Chloride Ions.—Table 3 shows the results of experiments carried out in the presence of chloride ions. The retardation of the rate by chloride is similar to that observed in the thallous–thallic exchange reaction [7] and in the reduction of thallium(III) by ferrous ion. As suggested by Harbottle and Dodson [7] this retardation is no doubt due

[6] Glasstone, Laidler, and Eyring, "The Theory of Rate Processes," McGraw-Hill, New York, 1941, Chap. 8.
[7] Harbottle and Dodson, *J. Amer. Chem. Soc.*, 1951, **73**, 2442.
[8] Zwolinski, Marcus, and Eyring, *Chem. Rev.*, 1955, **55**, 157.

to the formation of chloro-complexes of thallium(III), but there are insufficient data on these complexes to permit an analysis of the results.

Experimental

Stock Solutions.—Thallium(III) perchlorate was prepared by a method similar to that described by Ashurst and Higginson.[3] Thallium(III) oxide was reprecipitated twice before it was dissolved in 72% " AnalaR " perchloric acid. Total thallium(III) in the solution was determined by adding excess of a standard solution of ferrous sulphate and back-titrating the excess with standard potassium dichromate. The acid concentration of the thallium(III) solution was estimated as described by Johnson.[1]

Trisdipyridylosmium(II) perchlorate was prepared by Burstall, Dwyer, and Gyarfas's method.[9] A stock solution was made up by weight and checked by spectrophotometric titration with a standard solution of " AnalaR " ceric ammonium nitrate.

Sodium perchlorate solution used for adjusting ionic strength was prepared by neutralising " AnalaR " perchloric acid with " AnalaR " sodium hydroxide and filtering.

Conductivity water was used for all solutions; it was obtained by redistilling distilled water, to which a little alkaline potassium permanganate was added, in an all-glass apparatus. The redistilled water was then passed through a column of Permutit " Bio-deminrolit."

Procedure.—Solutions of trisdipyridylosmium(II) being intensely coloured, the reaction was followed spectrophotometrically at a wavelength of 480 mμ, at which the osmium(III) compound has practically no absorption. A simple flow system, in which water from a thermostat was circulated around the spectrophotometer cell holder, enabled the reaction to be carried out at constant temperature.

The recorded values of k_1 are the means obtained from two kinetic runs with two different preparations of thallium(III). The values of k_1 from the two experiments were found to be within 5% of each other.

At the high concentrations of perchlorate used some initial oxidation of the $Os(dipy)_3^{2+}$ was observed, which appeared to be due largely to some impurity in the sodium perchlorate solution, but a slight amount was also caused by the perchloric acid. Fortunately the oxidation occurred instantaneously, so that the kinetics were not affected if thallium(III) was added last to the reaction mixture. Its only effect then was to alter the initial concentration of $Os(dipy)_3^{2+}$, and by running a blank before each experiment the extent of the alteration could be determined. In no case did the amount of initial oxidation caused by the perchlorate solutions exceed 15%, so that never more than 15% of the tervalent osmium complex was present at the start of any given reaction.

Because of the low concentration of the reactants used [*ca.* $5{\cdot}0 \times 10^{-5}$M for the osmium compound and 10^{-4}M for thallium(III)] it seemed advisable to check the quantitativeness of the reaction under these conditions. Experiment showed that with $2{\cdot}16 \times 10^{-5}$M-thallium(III) and $4{\cdot}40 \times 10^{-5}$M-$Os(dipy)_3^{2+}$ and the initial oxidation of $Os(dipy)_3^{2+}$ in the high perchlorate medium being allowed for, 95% of the osmium compound was oxidised by the thallium(III).

All the experiments were conducted at a constant ionic strength of 2·99.

I thank Professor P. George for helpful criticisms and Professor C. W. L. Bevan for his interest.

University College, Ibadan, Nigeria. [*Received, November 19th,* 1956.]

[9] Burstall, Dwyer, and Gyarfas, *J.*, 1950, 953.

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348. *Structural Modifications of* β-NiO·OH.

By G. W. D. Briggs.

The existence of additional reflections in the *X*-ray diffraction pattern of β-NiO·OH is reported, and a modified form of the oxide obtained by electrodeposition in the presence of foreign ions is described.

The higher nickel oxides of composition near Ni_2O_3,xH_2O or NiO·OH were first described [1] in detail by Glemser and Einerhand in 1950. These authors distinguished three forms of NiOOH, designated α, β, and γ, of which β-NiO·OH was obtained by precipitation or by anodic deposition from an acetate-buffered nickel sulphate solution at room temperature. They obtained an *X*-ray powder pattern from the β-form showing three diffuse lines at 4·9, 2·42, and 1·4 Å, and regarded these as the 001, 100, and 110 reflexions from a hexagonal lattice derived from that of $Ni(OH)_2$. Whilst examining the electrolytically formed oxide in these laboratories we observed some additional features of the *X*-ray diffraction pattern and have also distinguished a modified form of the oxide.

Examples of the diffraction patterns obtained are shown in the Plate. They were taken with Ni-filtered Cu-$K\alpha$ radiation and a 6 cm. cylindrical camera, the oxide being contained in a glass capillary of 0·3 mm. bore. Plate *a* shows the diffraction pattern obtained from oxide of composition $Ni_2O_{3\cdot04},2\cdot6H_2O$ deposited on nickel from a 0·5N-solution of nickel nitrate made N in sodium acetate, at a constant current of about 10 mA/cm.^{2}. It has strong lines at 4·8, 2·44, and 1·41 Å, corresponding to those listed by Glemser and Einerhand; but it shows also a strong line at 9·5 Å, a weak line at 3·2 Å, and indications of a very weak reflection at about 1·2 Å, none of these being mentioned by Glemser and Einerhand. The 2·4 Å line is also unsymmetrical in shape, as shown by the photometer trace, Fig. *a*. It may, therefore, be a two-dimensional (*hk*) reflection from a random layer lattice,[2] although the appearance could also be due to the presence of another broad band near 2·0 Å.

If the oxide is deposited in a solution buffered with potassium instead of sodium acetate, or if potassium nitrate is simply added to the bath at a concentration of about N, the modified diffraction pattern shown in Plate *b* and Fig. *b* is obtained. This has a strong inner line as before, but the spacing is about 7·6 Å as compared with 9·5 Å for the normal preparation. The strong line at 4·8 Å is replaced by a very broad diffuse band usually showing indistinct peaks at about 4·8 and 3·5 Å, the remaining lines appearing as in the normal pattern (Plate *a*).

These results suggested experiments with the addition of other ions to the depositing solution and it was found that the normal pattern (Plate *a*) was obtained in the presence of Li^+, Ca^{2+}, and Sr^{2+}, whereas the modified pattern (Plate *b*) was obtained with K^+, Ba^{2+}, Cs^+. As similar conditions were used for the deposition of each oxide, it seemed unlikely that electrochemical factors could be directly responsible for the change in structure, and the oxides were therefore examined for possible retention of foreign ions. The material was deposited on a large nickel anode, washed by suspension in water, and rapidly dried *in vacuo*, the effectiveness of washing being judged by the amount of sodium retained by the samples. Nickel, barium, and strontium were estimated by standard gravimetric methods; active oxygen iodometrically; sodium, potassium, and calcium by flame photometer; and water contents were obtained by difference.

The results tabulated show that, whereas sodium could be removed fairly easily from the oxides by adequate washing, potassium, calcium, strontium, and barium appeared to be strongly retained, the proportion of barium being much the largest and amounting to about 1 Ba per 12 Ni atoms. Although calcium and strontium seemed to be retained in

[1] Glemser and Einerhand, *Z. anorg. Chem.*, 1950, **261**, 26, 42.
[2] Warren, *Phys. Rev.*, 1941, **59**, 693; Brindley, "*X*-Ray Structure and Identification of Clay Minerals," Mineralogical Society (Clay Minerals Group), London, 1951, p. 285.

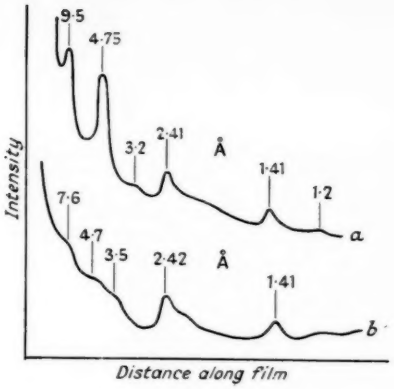
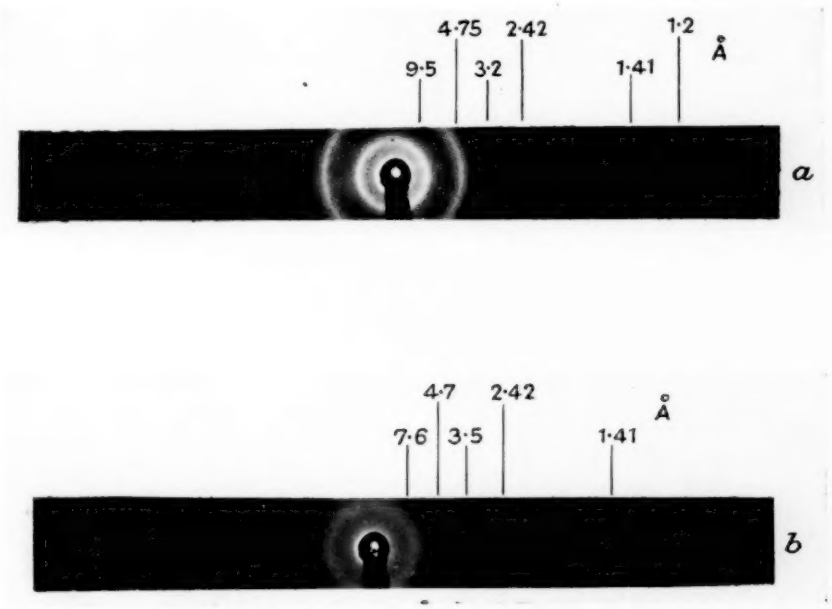


FIGURE. *Photometer traces corresponding to specimens a and b.*

PLATE. *Diffraction patterns of electrolytically deposited nickel oxides.*



[*To face p.* 1816.

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amounts comparable with those for potassium, the resulting oxides gave the normal diffraction pattern. This evidence suggests that the modified β-NiO·OH structure may be due to the retention by the oxide of relatively large ions. The possibility of a related change in the water content of the oxide, which considerably exceeds that required by the formula NiO·OH or Ni_2O_3,H_2O, is not excluded by our present evidence.

Solution used for deposition	Diff. pattern of oxide	Alkali-metal retained (%)	Compn. of oxide
0·5N-$Ni(NO_3)_2$ + N-NaOAc	Plate *a*	0·06	$Na_{0·005}Ni_2O_{3·03},2·6H_2O$
,, + N-$Ca(NO_3)_2$	,,	1·5	$Ca_{0·08}Ni_2O_{3·01},2·8H_2O$
,, + N-$Sr(NO_3)_2$	,,	1·5	—
,, + N-KNO_3	Plate *b*	1·23	$K_{0·09}Ni_2O_{3·94},2·7H_2O$
,, + satd. $Ba(NO_3)_2$	,,	9·3	$Ba_{0·17}Ni_2O_{3·17},3·3H_2O$

The additional lines observed in the *X*-ray diffraction pattern of β-NiO·OH may be accommodated by a slight modification to the indexing proposed by Glemser and Einerhand, since the spacings of 9·5, 4·8, 3·2, 2·4, 1·4, and 1·2 Å would correspond to the 001, 002, 003, 100, 110, and 200 reflections respectively from a hexagonal lattice with unit cell $a = 2·8$ Å and $c = 9·5$ Å. Although an adjustment of this kind is feasible, we feel that our results show the need for a fuller investigation of these oxides before a detailed account of their structure is attempted. For example, the existence of mixed layer lattices analogous to those formed by some groups of clay minerals, may be implied by the large and variable water contents of the oxides and by the changes in apparently prominent basal spacings brought about in the presence of large foreign ions.

The author thanks Professor W. F. K. Wynne-Jones for providing facilities and encouragement, Dr. H. P. Stadler for most helpful discussion of the *X*-ray results, Mr. J. Shaw for analyses of sodium, potassium, and calcium, and the Electricity Supply Research Council of the Central Electricity Authority for their support of this work.

King's College, University of Durham,
Newcastle upon Tyne, 1.

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349. *The Barium Fluoride–Uranium Trifluoride System.*

By R. W. M. D'Eye and F. S. Martin.

The system UF_3–BaF_2 has been examined by *X*-ray and density measurements and by thermal analysis. Uranium trifluoride dissolves in solid barium fluoride to the extent of about 50 mole %, the cell constant *a* decreasing from 6·189 to 6·034 kX; barium fluoride dissolves in uranium fluoride to the extent of about 20 mole %. These two conjugate solid solutions exist between definite concentration limits. It is also shown that uranium trifluoride may form a solid solution in strontium fluoride.

The melting point of uranium trifluoride is found to be about 1495°; its addition to barium fluoride increases the melting point of the latter, and it is suggested that the system has a peritectic point at about 1400°.

Vogt's [1] thermal analytical work indicated that 45 mole % of yttrium trifluoride could be dissolved in calcium fluoride. This was substantiated by Goldschmidt's [2] *X*-ray diffraction study of the mineral fluorite (Ca, Y)F_3. Goldschmidt suggested that in these mixed crystals the calcium and yttrium ions were randomly distributed over the normal cation sites of the fluorite-type lattice, *i.e.*, the positions 000, etc., in the unit cell, and that the extra fluoride ions needed for electric neutrality occupied, presumably statistically, the

[1] Vogt, *Neues Jahrb. Mineral.*, 1914, **2**, 9.
[2] Goldschmidt, *Geochem. Verteilungsgesetze*, 1926, **7**, 88.

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largest " holes " in the lattice, *i.e.*, the positions ½00, etc. The composition of the mixed crystals could also be accounted for if the cation lattice were incomplete, $2Y^{3+}$ replacing $3Ca^{2+}$, with the anion lattice intact. However, density and *X*-ray diffraction studies of the systems CaF_2–YF_3 ($Ca^{2+} = 0{\cdot}99$, $Y^{3+} = 0{\cdot}93$ kX), SrF_2–LaF_3 ($Sr^{2+} = 1{\cdot}13$, $La^{3+} = 1{\cdot}15$ kX), and CaF_2–ThF_4 ($Ca^{2+} = 0{\cdot}99$, $Th^{4+} = 1{\cdot}02$ kX) by Zintl and Udgård,[3] and of SrF_2–LaF_3 by Ketelaar and Willems,[4] proved that Goldschmidt's concept of interstitial anions and an intact cation lattice was correct. Results of our present study of the BaF_2–UF_3 system also agree with the interstitial anion theory.

For mixed-crystal formation Zintl *et al.*[3] considered that the cations in the component fluorides should have similar ionic radii. This is not necessarily the case. For example, our investigation of the BaF_2–UF_3 system ($Ba^{2+} = 1{\cdot}35$, $U^{3+} = 1{\cdot}04$ kX) shows that uranium trifluoride has an appreciable solid solubility in barium fluoride, mixed crystals with the fluorite-type structure being formed. We also have a single measurement which shows that uranium trifluoride and strontium fluoride ($Sr^{2+} = 1{\cdot}13$ kX) form mixed crystals.

Alberman and Anderson,[5] in their discussion of the effect of incorporating interstitial anions into a fluorite-type lattice, suggest that the net effect on the cell dimensions is determined by the interplay of the size and charge of the substituting cation with the distortion caused by the interstitial anion. Thus, if the radii of the cations are similar, the lattice-distortion effect will probably predominate, causing the cell to expand as the anion : cation ratio increases. This is true for the systems CaF_2–YF_3, SrF_2–LaF_3, and CaF_2–ThF_4. If, however, the substituting cation is smaller, as well as carrying a higher charge, these effects may outweigh the distortion effect of the interstitial anions and result in contraction of the cell as the anion : cation ratio increases. We find this is the case for the BaF_2–UF_3 system where the cell constant contracts from $a = 6{\cdot}189 \pm 0{\cdot}005$ kX for barium fluoride to $6{\cdot}034 \pm 0{\cdot}005$ kX for a mixed crystal containing 50 mole % of uranium trifluoride.

The incorporation of interstitial atoms into the positions ½00, etc., in a unit cell with the fluorite-type structure should enhance the intensity of diffraction planes with all indices even. However, these intensity changes should only be discerned when the scattering power of the cations and anions is comparable. Thus as expected, intensity changes were found in the CaF_2–YF_3 but not in the BaF_2–UF_3 system.

Solid Solubility Limits.—For the systems CaF_2–YF_3 and SrF_2–YF_3, mixtures containing more than 33·3 moles % of the trifluoride consisted of the cubic solid-solution phase and the hexagonal trifluoride.[3] However, no mention has been made of the possibility of solid solution of the difluoride in the trifluoride. With the CaF_2–ThF_4 system an unidentified phase plus the solid-solution cubic phase was found in mixtures containing between 27·3 and 50 moles % of thorium tetrafluoride. We suggest that this unidentified phase was $CaThF_6$ (cf. ref. 6).

We find that the solid solubility limit of uranium trifluoride in barium fluoride is roughly 50 moles %, corresponding to two interstitial anions per unit cell. Two phases were present in samples with a higher uranium trifluoride content; the cubic solid-solution phase and an hexagonal phase with cell dimensions only slightly larger than those for pure uranium trifluoride. The cell dimensions of the hexagonal phase decreased with increasing trifluoride content, suggesting a solid solution range of barium fluoride in uranium trifluoride.

The incorporation of barium fluoride into the uranium trifluoride lattice could be explained either if the cation lattice remained intact with, to preserve electric neutrality, a deficient anion lattice, or if the anion lattice remained intact with interstitial cations, $3Ba^{2+}$ replacing $2U^{3+}$. The latter possibility is unlikely in a close packed structure such

[3] Zintl and Udgård, *Z. anorg. Chem.*, 1939, **240**, 150.
[4] Ketelaar and Willems, *Rec. Trav. chim.*, 1937, **56**, 29.
[5] Alberman and Anderson, *J.*, 1949, S 305.

as uranium trifluoride.[6,7] In fact, calculations of packing and interatomic distance seem to preclude the idea of interstitial cations. Our density and *X*-ray diffraction data confirm this prediction.

Experimental

Uranium Trifluoride.—This was prepared by a method similar to that described by Warf [8] in which finely divided uranium powder is heated with the stoicheiometric quantity of uranium tetrafluoride in an inert atmosphere. *X*-Ray analysis showed that some products contained traces (<2%) of uranium dioxide.

Mixed Crystals.—These were prepared by heating intimate mixtures of barium fluoride and uranium trifluoride, in the requisite quantities, in graphite crucibles in an atmosphere of argon which was purified by passage through traps cooled with liquid oxygen and then over heated uranium turnings. The mixtures for *X*-ray analysis were heated for about 30 min. at 1300° and cooled fairly rapidly by removal from the furnace. Although graphite crucibles were used no evidence of carbide formation was found. Some melts had a thin skin of carbon which was readily scraped away. The mixed crystals rich in uranium trifluoride were deep purple-black, and those rich in barium fluoride were pinkish-brown.

Thermal Analysis.—Cooling curves were obtained on some of the samples by means of a Pt–13% Rh/Pt thermocouple inserted into a well in the base of the crucible. The samples were cooled at the rate of about 1° per min. by means of a motorised Variac transformer delivering power to a molybdenum resistance-wound heater. The graphite crucibles were thoroughly outgassed before use for an hour *in vacuo* at 1400—1500°.

X-Ray Diffraction.—For the *X*-ray examination of the mixed crystals we used a Guinier-type focusing camera [9] and monochromatised and focused Cu-K_α radiation from a bent quartz plate. To avoid shrinkage errors in the measurement of the Bragg angle θ, a 0·1 mm. scale was photographed on the film before processing.

Pyknometric Density.—Densities were calculated from the difference in weight of the mixed crystal in air and in toluene. To avoid low density values, through incomplete filling of the microcapillaries in the surface structure of the crystals, the pyknometric liquid was added to the solid under a vacuum. Both the solid and the toluene were thoroughly outgassed *in vacuo* before use.

Results and discussion

X-Ray and Density.—The values of the cell constant, a, for various mixed crystal compositions are shown in the Table. The cell constant decreases approximately linearly with increasing uranium trifluoride content down to the solid solubility limit of 50 moles %.

From these cell constants densities were calculated on the assumption of (i) interstitial anions with a complete cation lattice and (ii) a complete anion lattice with a defective cation lattice (see Table). The measured density corresponds closely to that calculated on the former basis.

At a composition of 66·66 moles % of uranium trifluoride the diffraction photograph shows that two phases were present; a fluorite phase with a cell parameter corresponding to that for the limit of solid solubility of uranium trifluoride in barium fluoride and a hexagonal phase with cell constants slightly larger than those for pure uranium trifluoride. This hexagonal phase is a solid solution of barium fluoride in uranium trifluoride, and its composition must correspond to the limit of solid solubility of the barium fluoride, about 20 moles %, in the trifluoride.

The mode of incorporation of the barium fluoride into the uranium fluoride has been determined from *X*-ray-diffraction and density measurements. For example, the density was calculated for a composition of 90 moles % of uranium fluoride both on the assumption

[6] Zachariasen, *Acta Cryst.*, 1949, **2**, 388.
[7] Staritzky and Douglas, *Analyt. Chem.*, 1956, **28**, 1056.
[8] Warf, A.E.C.D. 2413 (1948).
[9] D'Eye, A.E.R.E. C-R 1524 (1954); *Nature*, 1955, **175**, 623.

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(i) that the uranium and barium ions were randomly distributed over the normal cation sites, *i.e.*, the positions 6(*g*) $x0\frac{1}{4}$, etc. (space group $P6_3$ mcm),[7] in the unit cell, with the anion lattice incomplete, and (ii) that the anion lattice is complete, *i.e.*, the positions 2(*a*) $00\frac{1}{4}$, etc., 4(*c*) $\frac{1}{3}\frac{2}{3}\frac{1}{4}$, etc., 12(*k*) *x*0*z*, etc., in the unit cell, with interstitial cations to preserve the charge balance. The calculated densities for these two possibilities are respectively 8·52 and 8·81 g./c.c. The measured density is 8·50 g./c.c., in good agreement with the density calculated on the assumption (i) above of vacant anion sites. Further weight to this anion-vacancy mechanism is given by considerations of interatomic distances which show that the lattice is unlikely to accommodate interstitial cations.

BaF_2–UF_3 *anomalous mixed crystals.*

BaF_2 (moles %)	*a* (± 0·005) (kX)	*d*, calc. on interstitial anions (g./c.c.)	*d*, calc. on vacant cations (g./c.c.)	Measured density (g./c.c.)	Remarks
100	6·189	—	—	4·85	
93·8	6·169	5·14	4·99	5·07	
87·06	6·139	5·45	5·11	5·45	
80·00	6·137	5·69	5·17	5·74	
75·00	6·110	5·94	5·28	5·87	
66·66	6·079	—	—	—	
50·00	6·034	—	—	—	
33·33	6·035	—	—	—	Minor phase, cubic; major phase, hexagonal; *a* = 4·197; *c* = 7·359
10	—	—	—	—	Single hexagonal phase; *a* = 4·153; *c* = 7·329
0	—	—	—	—	Hexagonal UF_3; *a* = 4·131; *c* = 7·335

A sample of composition 33·3 moles % of UF_3 in SrF_2 had $a = 5{\cdot}821 \pm 0{\cdot}005$ kX.

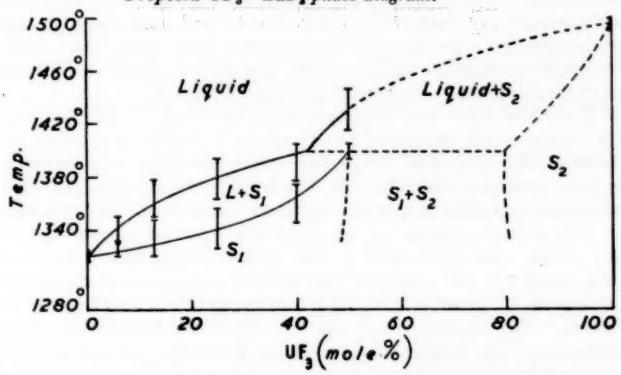
If the variable parameter for the cation positions is exactly $x = \frac{1}{3}$, the structure can be considered to be made up of layers of uranium and fluorine ions with each uranium surrounded by three equidistant fluoride ions and each fluorine ion surrounded by three equidistant uranium ions. These fluoride ions occupy the positions 2(*a*) and (4(*c*) in the unit cell. Above and below each uranium there is a further fluoride ion. These fluoride ions, which sit between the layers, occupy the positions 12(*k*) in the unit cell. The fluoride ions in the layers have three nearest uranium neighbours whereas those between the layers only have one nearest uranium neighbour. Thus the fluoride ions in the layers are not structurally equivalent to those between the layers.

Therefore it is possible that the anion vacancies generated to accommodate the barium fluoride in the uranium trifluoride lattice are not statistically distributed over all the anion sites but are concentrated in either the positions 2(*a*) and 4(*c*), *i.e.*, the positions in the layers, or 12(*k*), *i.e.*, the positions between the layers.

Cooling Curve Results.—Most of the cooling curves had the expected feature of a change of slope bounded by two points of inflection corresponding to liquidus and solidus points. In one case (50 moles % of UF_3), the second point of inflection (solidus) was followed by a horizontal section on the curve; this denoted the presence of an invariant system at this point. The reproducibility of the points was not very good; *X*-ray analysis of those samples which had been held at 1400—1500° for an extended period (as in cooling at 1° per min.) showed the presence of $BaUF_6$. This must have been formed by way of disproportionation of UF_3, *i.e.*, $4UF_3 \longrightarrow 3UF_4 + U$, and its presence would account for the rather indistinct points of inflection in the cooling curves. Disproportionation in the mixtures was not serious at about 1300°; for pure uranium trifluoride it was minimised by rapid heating to about 1480°, and the heating and cooling curves being then observed over the range 1480—1510°. At about 1500° approximately 20% of the trifluoride disproportionated in 1 hr.

The points of inflection are shown in the Figure. The *X*-ray diffraction results have shown that there is no compound formation in the BaF_2–UF_3 system and that two conjugate solid solutions may exist between certain concentration limits. It is therefore possible to have three phases present (two solid and one liquid), the system having in

Proposed UF_3—BaF_2 *phase diagram.*



S_1 = *Solid solution of* UF_3 *in* BaF_2. S_2 = *Solid solution of* BaF_2 *in* UF_3.

consequence an invariant point. The thermal data for the equimolar UF_3–BaF_2 mixture suggest that this point is about 1400°. In view of this we suggest that the system is of the peritectic type and we propose the phase diagram shown in the Figure.

We thank R. E. Brown for some experimental work, Mrs. G. W. Stuart for taking the *X*-ray diffraction photographs, and I. F. Ferguson for the density measurements.

Atomic Energy Research Establishment,
Harwell, nr. Didcot, Berks.

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350. *Thermochemistry of Organophosphorus Compounds. Part III.* The Heat of Addition of Sulphur to Triethyl Phosphite, and to Tri-n-propyl- and Tri-n-butyl-phosphine.*

By C. L. Chernick, J. B. Pedley, and H. A. Skinner.

The heats of addition of rhombic sulphur to excess of liquid triethyl phosphite, and to liquid tri-*n*-propyl- and tri-*n*-butyl-phosphine have been measured at 25°, $\Delta H_{obs.} = -26{\cdot}6$, $-27{\cdot}6$, and $-27{\cdot}5$ kcal./mole respectively. From these heats, and the assumed value $\Delta H_f°$ (*S*, g.) ~66 kcal./mole, the heats of disruption of the thiophosphoryl bonds are derived, *viz.*: $D(S{=}PR_3)$ ~90·6, 91·6, and 91·5 kcal./mole for R = OEt, Pr^n, and Bu^n respectively. It is suggested that the degree of multiple bonding (bond order) is less in thiophosphoryl than in phosphoryl bonds.

According to Strecker and Spitaler,[1] sulphur adds directly to triethyl phosphite to form triethyl thionophosphate readily at room temperature, $(EtO)_3P + S \longrightarrow SP(OEt)_3$. Kosolapoff [2] states that a similar direct addition occurs with the trialkylphosphines, to form the trialkylphosphine sulphides. In this paper we report on the heats of addition of sulphur to triethyl phosphite and to tri-*n*-propyl- and tri-*n*-butyl-phosphine, measured

* Part II, *J.*, 1956, 1041.

[1] Strecker and Spitaler, *Ber.*, 1926, **59**, 1772.
[2] Kosolapoff, "Organophosphorus Compounds," John Wiley, New York, 1950, p. 235.

directly from the heat evolved on dissolving pure rhombic sulphur in an excess of each of these liquids.

Experimental

Preparations.—Triethyl phosphite was prepared by the method of Ford-Moore and Perry.[3] The crude product was fractionally distilled under reduced (nitrogen) pressure through an 8″ gauze-packed column. The fraction, b. p. 36·0°/3 mm., was retained. Tri-*n*-propyl- and tri-*n*-butyl-phosphine were prepared according to Davies and Jones [4] and Davies, Pearse, and Jones.[5] The crude products were purified by fractional distillation under reduced (nitrogen) pressure. The fractions retained had b. p. 60—62°/2 mm. (PPr_3) and 68—70°/0·5 mm. (PBu_3). A sample of pure rhombic sulphur was provided by Mr. G. Merrall.

Calorimeter.—The calorimeter will be described in detail elsewhere, and is similar to that used by Chernick, Skinner, and Wadsö.[6] It consists of a Dewar vessel contained in a copper cylindrical can fitted with a flanged lid, and when in use, is totally immersed in a thermostat at 25·0°. A Pyrex-glass reaction vessel (30 ml. capacity) is supported centrally in the Dewar vessel by an arm which emerges through the lid of the calorimeter and attached externally to a Vibro-shaker. The reaction vessel can be vigorously agitated in the water surrounding it inside the Dewar vessel. The procedure in the present experiments was as follows: The reaction vessel was swept out with nitrogen and charged with a known excess of the phosphine derivative. A thin glass ampoule containing a known weight of sulphur was held in position in the reaction vessel. The reaction vessel was then fitted into the calorimeter, and the Vibro-shaker set in oscillation. On attainment of a steady state, the fore-rating curve was plotted from the change in resistance with time of a shielded thermistor element immersed in the water (375 g.) contained in the Dewar vessel. The ampoule was then broken, and the ensuing resistance change plotted until reaction ceased. After this the system re-attained a steady state, and the post-rating curve was plotted.

Reaction between the trialkylphosphines and sulphur is rapid, being complete in <5 min. The sulphur–triethyl phosphite reaction proved more troublesome, for, although reaction begins rapidly, it approaches the end-point sluggishly, and reaction times of 20—30 min. were required. In a few experiments, particles of undissolved sulphur still remained visible in the contents of the reaction vessel at the " end " of the experiment. The results obtained in " unfinished " experiments were discarded.

The calorimeter was calibrated electrically by the substitution method. The experiments were carried out at 25°, and all heat quantities are quoted in thermochemical calories, defined by 1 calorie ≡ 4·1840 abs. joules.

Results.—The observed heats of reaction, $\Delta H_{obs.}$, are given in the following Tables, and relate to the general equation:

$$PR_3\ (liq.) + S(c.) \longrightarrow SPR_3\ (soln.\ in\ PR_3) \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where R = OEt, Pr^n, and Bu^n.

Table 1. *Heat of addition of sulphur to triethyl phosphite.*

Expt.	Sulphur (g.)	$-\Delta H_{obs.}$ (kcal./mole)	Expt.	Sulphur (g.)	$-\Delta H_{obs.}$ (kcal./mole)
1	0·5002	26·6	4	0·4018	26·9
2	0·5000	26·2	5	0·3381	27·1
3	0·3780	26·1			

Mean $\Delta H_{obs.} = -26·6 \pm 0·4$ kcal./mole.

Table 2. *Heat of addition of sulphur to* PPr_3 *and to* PBu_3.

	(*a*) PPr_3 + S.			(*b*) PBu_3 + S.	
Expt.	Sulphur (g.)	$-\Delta H_{obs.}$ (kcal./mole)	Expt.	Sulphur (g.)	$-\Delta H_{obs.}$ (kcal./mole)
1	0·3920	27·5	1	0·4124	27·9
2	0·4072	27·6	2	0·3812	26·9
3	0·3930	27·6	3	0·4030	27·7
Mean $\Delta H_{obs.} = -27·6 \pm 0·1$			Mean $\Delta H_{obs.} = -27·5 \pm 0·4$		

[3] Ford-Moore and Perry, *Org. Synth.*, 1951, **31**, 111.
[4] Davies and Jones, *J.*, 1929, 33.
[5] Davies, Pearse, and Jones, *J.*, 1929, 1262.
[6] Chernick, Skinner, and Wadsö, *Trans. Faraday Soc.*, 1956, **52**, 1088.

Discussion

From the $\Delta H_{obs.}$ values in Tables 1 and 2, together with certain other thermal data, we may derive values for the heats of disruption of sulphur–phosphorus bonds in SPR_3 molecules. The thermal data required, in addition to $\Delta H_{obs.}$, are the heats of vaporization of PR_3 and SPR_3, the heats of solution of SPR_3 in liquid PR_3, and the heat of atomization of rhombic sulphur, since :

$$D(S{=}PR_3) = \Delta H_f^\circ(S, g.) - \Delta H_{obs.} + \Delta H_{vap.}(PR_3) - \Delta H_{vap.}(SPR_3) + \Delta H_{soln.} \quad (2)$$

where $D(S{=}PR_3)$ symbolizes the bond dissociation energy of the sulphur–phosphorus bond in SPR_3.

The heat of formation of atomic sulphur is not yet settled, and several values for it have been proposed. One of the most useful methods of arriving at $\Delta H_f^\circ(S, g.)$ is from changes in heat content (ΔH_1 and ΔH_2) of the processes (*a*) and (*b*) respectively :

$$(a)\ S\ (\text{rhombic}) \longrightarrow S_2\ (g.);\ \Delta H_1$$

$$(b)\ S_2\ (g.) \longrightarrow 2S\ (g.);\ \Delta H_2$$

whence, ΔH_f°, $(S, g.) = \frac{1}{2}(\Delta H_1 + \Delta H_2)$.

Evans and Wagman [7] concluded that the " best " value for ΔH_1 is 30·8 kcal./mole, obtained from measurements of the dissociation of hydrogen sulphide at high temperatures. The " best " value for ΔH_2 is not easily chosen, and Gaydon [8] considers that there are 3 possible values (3·3, 3·6, and 4·4 ev), from among which he prefers the highest, *i.e.*, $\Delta H_2 = 101$ kcal./mole. On the other hand, a recent investigation by St. Pierre and Chipman [9] led them to conclude that $\Delta H_2 = 83$ kcal./mole.

For the present purpose, we have accepted the values $\Delta H_1 = 30{\cdot}8$ and $\Delta H_2 = 101$, leading to $\Delta H_f^\circ(S, g.) \sim 66$ kcal./mole. Of the remaining items in eqn. (2), data are completely lacking in respect of $\Delta H_{vap.}(SPR_3)$, and are not well-established in respect of $\Delta H_{vap.}(PR_3)$, but it is unlikely that the difference, $\Delta H_{vap.}(SPR_3, liq.) - \Delta H_{vap.}(PR_3)$, is appreciably in excess of 2 kcal./mole. The term in $\Delta H_{soln.}$ is small : in the case of $SPPr_3$, we prepared a pure sample, and measured the heat of mixing with PPr_3, finding $\Delta H_{soln.}$ to be almost negligible (<0·1 kcal./mole). Hence, we may rewrite eqn. (2) approximately, as :

$$D(S{=}PR_3) \sim 64 - \Delta H_{obs.} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

to give :

$$D[S{=}P(OEt)_3] \sim 90{\cdot}6 \text{ kcal./mole}$$

$$D(S{=}PPr_3) \sim 91{\cdot}6 \text{ kcal./mole}$$

$$D(S{=}PBu_3) \sim 91{\cdot}5 \text{ kcal./mole}$$

These values show that the $S{=}PR_3$ bond dissociation energies are markedly less than the related $O{=}PR_3$ dissociation energies, for which values were reported in Part II of this series.[10] Moreover, it would seem that the *increase* in strength of the phosphoryl bond over singly bonded phosphorus to oxygen is *ca.* twice as large as the increase in passing from S–P to S=P. [Chernick, Skinner, and Mortimer [11] obtained $D(P{-}OR) \sim 80$ kcal./mole, and, in Part II, values of $D(O{=}PR_3)$ were found to be >135 kcal./mole. The strength of the P–S single bond has not been measured directly, but can be estimated at *ca.* 64 kcal./mole from the relation between excess of ionic energy (Pauling [12]) and electronegativity difference. Hence the difference between

[7] Evans and Wagman, *J. Res. Nat. Bur. Stand.*, 1952, **49**, 141.
[8] Gaydon, " Dissociation Energies," Chapman and Hall, London, 1953, p. 205.
[9] St. Pierre and Chipman, *J. Amer. Chem. Soc.*, 1954, **76**, 4787.
[10] Chernick and Skinner, *J.*, 1956, 1401.
[11] Chernick, Skinner, and Mortimer, *J.*, 1955, 3936.
[12] Pauling, " Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, 1939, p. 60.

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O=P and O–P is *ca.* 55 kcal./mole, compared with *ca.* 26 kcal./mole between S=P and S–P]. A possible explanation is one that ascribes a greater degree of multiple-bond character to phosphoryl than to thiophosphoryl bonds, and is supported by Siebert's [13] finding, from force-constant measurements, that the O=P bond order in $OPCl_3$ is 2·09 against 1·57 for the S=P bond order in $SPCl_3$. This explanation is in line with a more general suggestion by Baddeley.[14]

Comment was made in Part II on the finding that $D(O{=}PR_3)$ varies appreciably with changes in the atom, or group, R, and the authors expressed some doubt in respect of the assumptions made in interpreting their thermochemical results. The present study, in contrast, reveals that the $D(S{=}PR_3)$ values remain almost unchanged on changing the group R, and re-emphasizes the need for an independent verification of the earlier conclusions in respect of phosphoryl bond dissociation energies.

THE UNIVERSITY, MANCHESTER. [*Received, December* 11*th*, 1956.]

[13] Siebert, *Z. anorg. Chem.*, 1954, **275**, 210.
[14] Baddeley, *J.*, 1950, 663.

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351. *Reactions of the Cobaltic Ion. Part IV.* The Oxidation of Olefins by Cobaltic Salts.*

By C. E. H. BAWN and J. A. SHARP.

The kinetics of the reaction of cobaltic ion with eight unsaturated hydrocarbons (2-methylbut-2-ene, pent-2-ene, hex-1-ene, hept-1-ene, oct-1-ene, 2-ethylbut-1-ene, styrene, and isoprene) in dilute sulphuric acid obey a second-order rate law, and it is shown that the primary reaction is the direct attack of the cobaltic ion at the double bond by electron transfer with the formation of a reactive radical ion :

$$R{\cdot}CH{=}CH_2 + Co^{3+} \longrightarrow R{\cdot}\dot{C}H{-}\overset{+}{C}H_2 + Co^{2+}$$

The secondary reaction to give the observed products (aldehydes, ketones, acids, and small amounts of diene) results from a series of reactions in which the carbonium ion reacts with water to give hydroxylic compounds which are then rapidly oxidised by the cobaltic ion in successive stages until stable products are formed. The energetics of the primary process are discussed.

COBALT salts are extensively used as catalysts in the autoxidation of aldehydes and saturated and unsaturated hydrocarbons and in these reactions the cobalt is usually used in the form of the salt of an organic acid which is soluble in the organic substrate. Studies of the oxidation by molecular oxygen of aldehydes and unsaturated hydrocarbons in glacial acetic acid with cobaltous acetate as catalyst have established that the activity of the catalyst resides in the higher-valency cobaltic state which is formed during the oxidation.[1] Other studies have shown that the cobaltic ion readily undergoes electron-transfer with a wide variety of organic molecules forming a free radical [2] and it is the latter reaction which is the initial stage in the oxidation processes. In order to elucidate the catalytic effect of cobalt salts in autoxidation the kinetics and mechanism of the reaction between cobaltic ion and olefins in dilute acid solution have been studied. In the following papers results are reported for the corresponding measurements in glacial acetic–sulphuric acid mixtures and for the reaction of cobaltic salts with hydroperoxides.

* Part III, *J.*, 1951, 344.

[1] Bawn, Tipper, and Pennington, *Discuss. Faraday Soc.*, 1951, **10**, 282; Bawn, *ibid.*, 1953, **14**, 181; Bawn and Williamson, *Trans. Faraday Soc.*, 1951, **47**, 721, 735.
[2] Bawn and White, *J.*, 1951, 311, 339, 344; Hargreaves and Sutcliffe, *Trans. Faraday Soc.*, 1955, **51**, 786.

Experimental

Cobaltic sulphate was prepared by the method of Swann and Xanthakos [3] and stored in a dark bottle at 0°.

2-Methylbut-2-ene was obtained by dehydration of *n*-pentyl alcohol with its own volume of 48% sulphuric acid at 80°; the hydrocarbon which distilled off was dried ($CaCl_2$), fractionated (b. p. 38·4° ± 0·1°/760 mm.), and stored at −78° under nitrogen.

Pent-2-ene was isolated from technical pentene by stirring it with its own volume of 50% sulphuric acid for 5 hr. at 0° to dissolve 2-methylbut-1- and -2-ene. The insoluble hydrocarbon was washed with a saturated solution of sodium hydrogen carbonate, dried ($CaCl_2$), and fractionated; the fraction boiling at 36·4° ± 0·5°/760 mm. was collected and stored under nitrogen at −78°.

2-Ethylbut-1-ene (from Messrs. Light) was washed with a saturated solution of sodium hydroxide, dried ($CaCl_2$), and fractionated. The hydrocarbon distilling over at 66·6° ± 0·2° was collected.

Styrene and isoprene were purified from stabiliser by washing them with a saturated solution of potassium hydroxide, followed by distillation under reduced pressure.

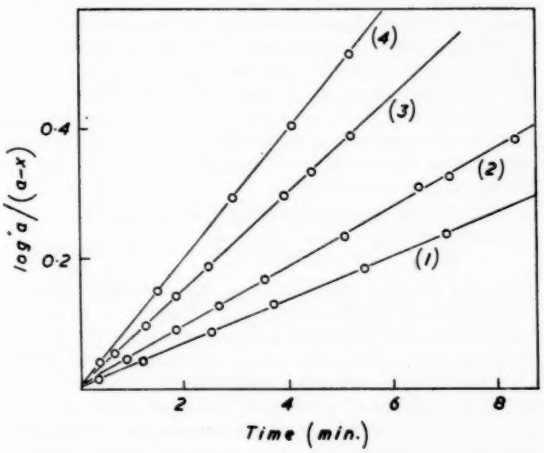

FIG. 1. *First-order plot for reduction of cobaltic sulphate by 2-methylbut-2-ene in 0·09M-sulphuric acid at 23·2°.*

$\mu = 0·112$, $a = 10^{-4}$M. Concentrations of olefin: (1) $0·76 \times 10^{-3}$M, (2) $1·04 \times 10^{-3}$M, (3) $1·71 \times 10^{-3}$M, (4) $2·27 \times 10^{-3}$M.

Hex-1-ene, hept-1-ene, oct-1-ene, and 2 : 4 : 4-trimethylpent-2-ene, presented by Imperial Chemical Industries Limited, Billingham Division, had been fractionated with high-precision stills. They were freed from hydroperoxide impurity by shaking them either with a saturated solution of sodium hydroxide or by passage through alumina.

Other materials used in this work were " AnalaR," not further purified.

Apparatus.—The reaction vessel consisted of a cylindrical quartz cell, length 10 cm. and diameter 1·5 cm., encased in a brass jacket through which water at a controlled temperature (within ±0·03° for temperatures from 12° to 45°) was pumped at a rate of 2 l. per min. The cell could be fixed into supports between the cell housing and photocell box of the Unicam spectrophotometer.

Analysis.—Olefin. Standard solutions of olefin were prepared by dissolving known volumes in water. To obtain the limits of solubility and to check the concentration of the solution the two following methods were used: (1) Olefins in aqueous solution absorb strongly in the range 180—210 mμ and the absorption was found to be proportional to the olefin concentration. Addition of 20% of ethyl alcohol enabled olefin concentrations greater than the maximum solubility in water to be determined. In these determinations the spectrum was measured against a corresponding alcohol–water blank. (2) The olefin was extracted from a known volume of aqueous solution by shaking it with a weighed quantity of Nujol (ratio Nujol : olefin *ca.* 15 : 1) and the refractive index of the solution measured with an Abbé refractometer. This

[3] Swann and Xanthakos, *J. Amer. Chem. Soc.*, 1931, **53**, 400.

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method gave results accurate to ±3% for aqueous solutions and was used largely to check the much more accurate absorption method.

Cobaltic salts. In the absence of olefins, cobaltic ion was determined by addition of excess of standard ferrous ion and back titration either with potassium permangante, the end point being determined potentiometrically by the differential titration method of Garman and Droz,[4] or with ceric sulphate, the indicator being *o*-phenanthroline. In the presence of the olefin and its oxidation products the permanganate method could not be used and the cobaltic-ion concentration was determined by light absorption. The absorption spectra of cobaltic sulphate solutions whose concentration had been determined by the above analytical procedures were measured from 200 mμ to 1000 mμ and shown to obey Beer's law. By use of this method solutions containing 10^{-5}—10^{-1}M-cobaltic ion could be determined within ±0·5% in the presence of olefins and the oxidation products. This method was used for all solutions whose extinction curves were known.

Procedure.—A standard aqueous solution of sulphuric acid–sodium hydrogen sulphate was shaken with sufficient olefin to saturate the solution. The solution was syphoned free from undissolved olefin and the olefin estimated. A known small volume of standard cobaltic sulphate in dilute sulphuric acid was shaken with a known volume of standard olefin solution, the mixture poured into the reaction cell, the cell placed in position, and the optical density measured within 10 sec. of mixing the two solutions and subsequently at ten-second intervals.

Reaction-rate Measurements.—In the presence of a large excess of olefin, the rate of disappearance of cobaltic ion was found to be accurately of the first order (Figs. 1 and 2), the first-order constants, $k_{obs.}$, being a linear function of the olefin concentration (Fig. 3) ($a = [Co^{3+}]_{initial}$, $x = [Co^{3+}]$ at time t). All the olefins investigated obeyed these relations. The plot of rate constant against olefin concentration intercepted the rate axis at the value corresponding to the reduction of cobaltic sulphate by the water. In sufficiently acid solutions the latter reaction was negligible.

The reaction rate may therefore be expressed

$$-d[Co^{3+}]/dt = k[Co^{3+}][\text{olefin}] + k'[Co^{3+}][\text{water}]$$

Thus the velocity constant, $k_{obs.}$, for the consumption of cobaltic ion at a fixed olefin concentration will be given by $k_{obs.} = k[\text{olefin}] + k'[\text{water}]$. Since $k'[\text{water}]$ is constant for any temperature and sulphuric acid concentration the second-order rate constant k can be obtained from the slope of the plot of $k_{obs.}$ against olefin concentration as shown in Fig. 3.

Effect of ionic strength. In 0·09M-sulphuric acid increase of the ionic strength μ from 0·11 to 2·0 by addition of potassium hydrogen sulphate (the salt being assumed to exist entirely as K^+ and HSO_4^- ions) reduced the bimolecular rate constant by 17%, showing that primary salt effects were absent. The rate constants for the different olefins were compared at a constant value of μ = 2·0.

Effect of oxygen and cobaltous sulphate. In view of the catalysis of the autoxidation of olefins by cobalt salts experiments were carried out both with carefully de-aerated solutions and in the presence of air. These showed that the presence of atmospheric oxygen in the solutions did not affect the kinetics. Cobaltous sulphate—the product of the oxidation—also had no influence on the reaction. An increase in the concentration of added cobaltous sulphate from zero to 0·1 mole/l. (*i.e.*, 10^3 × initial cobaltic concentration) did not affect the rate constant.

TABLE 1.

Temp. = 23·20°. Ionic strength = 2·0. $a = 10^{-4}$ g.-ion/l.

$[H_2SO_4]$	0·09	0·31	0·45	0·825	1·75	2·0
10^3[2-methylbut-2-ene]	1·08 × 10^{-3}	0·926	1·03	0·97	0·48	0·71
k (l. mole^{-1} sec.$^{-1}$)	1·34	1·29	1·19	1·56	1·29	1·42

Variation of hydrogen-ion concentration. For a series of sulphuric acid solutions of both oct-1-ene and 2-methylbut-2-ene, variation of the acid concentration from 0·09M to 2M at constant ionic strength 2 had no effect on the rate (Table 1). The rate of reduction of the cobaltic sulphate was therefore not affected by the change in hydrogen-ion concentration.

Variation of rate with olefin structure. The values of the second-order rate constants for the

[4] Garman and Droz, *Analyt. Chem.*, 1939, **11**, 398.

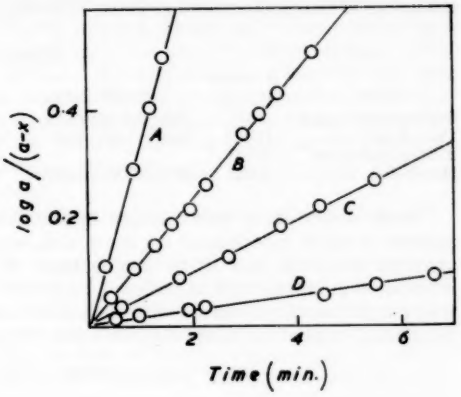

FIG. 2. *Variation of rate of reduction of cobaltic sulphate by hexene with temperature in 0·09M-sulphuric acid.*

$\mu = 0{\cdot}112$, $a = 10^{-4}$M. *A*, 44·1°; *B*, 37·4°; *C*, 30·60°; *D*, 24·85°.

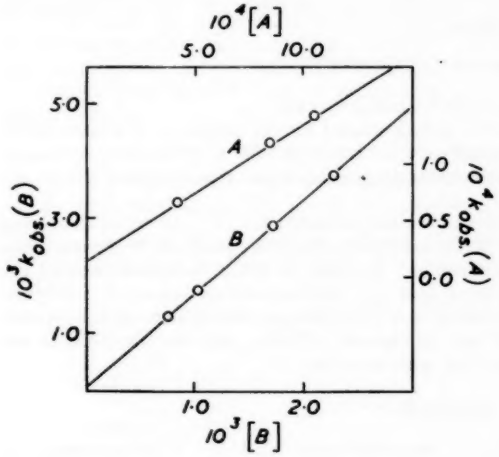

FIG. 3. *Dependence of rate of reduction of cobaltic ion on olefin concentration in 0·09M-sulphuric acid.*

A, Oct-1-ene at 19·8°; *B*, 2-methylbut-2-ene at 23·2°. $10^3 k_{obs.} = -$ d ln x/dt (sec.$^{-1}$).

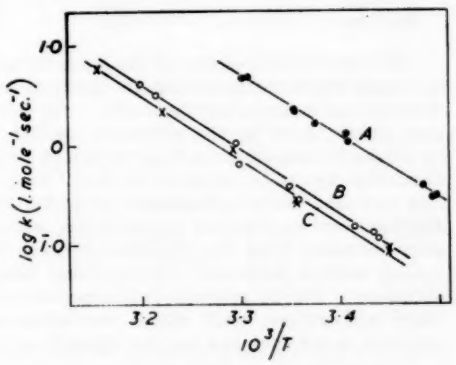

FIG. 4. *Temperature variation of rate of reduction of cobaltic ion by three olefins in 0·09M-sulphuric acid* ($\mu = 0{\cdot}112$).

A, 2-Methylbut-2-ene; *B*, oct-1-ene; *C*, hex-1-ene.

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reduction of cobaltic sulphate by eight olefins were measured in 0·09M-sulphuric acid at 25°; the values of the constants are given in Table 2 ($\mu = 2·0$).

TABLE 2.

Olefin	k (l. mole^{-1} sec.$^{-1}$)	Type of olefin	Olefin	k (l. mole^{-1} sec.$^{-1}$)	Type of olefin
2-Methylbut-2-ene	2·19	Trialkyl-ethylene	Hept-1-ene	0·368	Monoalkyl-ethylene
Pent-2-ene	0·903	Dialkyl-ethylene	Oct-1-ene	0·369	,, ,,
2-Ethylbut-1-ene	0·751	,, ,,	Styrene	7·38	Phenyl-ethylene
Hex-1-ene	0·321	Monoalkyl-ethylene	Isoprene	6·20	Conjugated diene

These results show that increase in reactivity of the olefin occurs (*a*) on increasing the number of alkyl substituents on the double-bonded carbon atoms, (*b*) by introduction of an aromatic grouping, and (*c*) by conjugation. It was not possible to determine directly the influence of groupings such as carboxyl, hydroxyl, etc., on the reactivity of the double bond since preferential reaction occurred with the substituent grouping. Thus oxidation of crotonic acid by cobaltic sulphate in dilute sulphuric acid obeyed the rate relationship

$$-d[Co^{3+}]/dt = 0·0108[Co^{3+}][CH_3·CH=CH·CO_2H]/[H^+]$$

at 25° showing that the crotonate ion was attacked by the cobaltic ion; by comparison, the oxidation at the double bond occurs at a negligible rate. Substitution of the dissociation constant of crotonic acid in the above equation gives

$$d[Co^{3+}]/dt = 494[Co^{3+}][CH_3·CH=CH·CO_2^-]$$

The corresponding value of k for the formate ion [2] reaction was 161.

Temperature coefficient. The second-order rate constants for the oxidation of 2-methylbut-2-ene, oct-1-ene, and hex-1-ene were measured over the range 16—36° and the three Arrhenius plots are shown in Fig. 4. The values of the activation energies and the frequency factors are summarised in Table 3.

Products of Olefin Oxidation.—On account of the low solubility ($\sim 2·0 \times 10^{-3}$M) of the olefins in aqueous solution it was not possible to isolate and characterise the products of the oxidation under the conditions of the kinetic measurements. In order to obtain sufficient product the cobaltic sulphate solution in 2—10N-sulphuric acid was shaken with an excess of (insoluble) olefin (progressive solution of the olefin occurring as the reaction proceeded) until all the cobaltic ion had reacted. The products from 200 ml. of aqueous solution and any dissolved in the relatively small volume of unoxidised olefin film were analysed.

TABLE 3.

Olefin	k at 25° (l. mole^{-1} sec.$^{-1}$)	E (kcal./mole)	A	S^* (cal./deg.)
2-Methylbut-2-ene	2·19	27·1 (±0·4)	$1·6 \times 10^{20}$	32·2
Oct-1-ene	0·369	28·5 (±0·9)	$3·1 \times 10^{20}$	33·6
Hex-1-ene	0·321	29·0 (±0·4)	$5·9 \times 10^{20}$	34·8

With most of the olefins all the products were volatile. The aqueous solution was distilled in a small fractionating column, the products being collected at 0°. Each successive 10% of the distillate was analysed independently. Glycols, which would not distil under these conditions, were sought both by the periodate–arsenite method [5] and by periodate oxidation followed by aldehyde determination [6] and shown to be absent. Formaldehyde was determined before distillation by use of chromotropic acid [7] since heating in the presence of olefin and sulphuric acid may lead to its partial removal by the Prins condensation. Individual fractions of the distillate were analysed for organic acids, aldehydes, and ketones as follows: (*a*) Acids (total) were estimated from the difference between the sulphuric acid as determined by titration against sodium hydroxide (bromophenol blue) and the total acid concentration (phenolphthalein). Formic acid was determined by reduction to formaldehyde (with magnesium and dilute hydrochloric acid) which was estimated by the chromotropic acid method. The reduction is not complete and the method was calibrated for the formic acid concentrations in

[5] Reinke and Luce, *Ind. Eng. Chem.* (*Anal.*), 1946, **18**, 244.
[6] Feigl, "Spot Tests," Elsevier, New York, 3rd edn., 1947, p. 326.
[7] Bricker and Johnson, *Ind. Eng. Chem.* (*Anal.*), 1945, **17**, 400.

the range $5{\cdot}0 \times 10^{-4}$M to 10^{-2}M. Under fixed conditions of reduction the ratios of formic acid reduced to formaldehyde produced was reproducible within ±5%. (*b*) Acetaldehyde was detected in the presence of formaldehyde by the red colour produced and by its reaction with diazobenzenesulphonic acid. Measurement by absorption was accurate only to within ±25% owing to the low extinction coefficient of the product. A semiquantitative method dependent on the coloration in Schiff's reaction in neutral solution followed by light absorption determination agreed with results of the first method in that acetaldehyde accounted for less than 0·5% of the products. (*c*) Ketones were identified by isolation as 2 : 4-dinitrophenylhydrazones. Quantitative determination of ketone was effected by measuring the acid liberated when the ketone reacted with hydroxylamine hydrochloride.[8]

These general analytical procedures were supplemented by specific methods of identification and estimation as described below.

Analytical Results.—2-Methylbut-2-ene. A series of product determinations are summarised in Table 4. The ketone was identified as acetone; its 2 : 4-dinitrophenylhydrazone whose spectrum and m. p. agreed with the literature data. The absorption spectrum of one of the distillates showed a strong absorption maximum at 230 mμ characteristic of a conjugated system. This product was not formed by the interaction of 2N-sulphuric acid and the hydrocarbon, nor was it initially present as an impurity. Its identity as isoprene was established by (*a*) comparison of its absorption spectra with that of isoprene in water and ether, (*b*) determination of the partition between water and ether, and (*c*) the rate of polymerisation in aqueous solution as determined by the rate of decrease of maximum optical density. The formation of formaldehyde and formic acid also provided indirect evidence for the formation of isoprene since the latter is readily oxidised to these products by cobaltic sulphate.

The analyses indicate that the following simultaneous oxidations occur in the presence of excess of olefin :

$$Me_2C{:}CHMe + Co^{3+} \longrightarrow Me_2CO + Me{\cdot}CHO + Me{\cdot}CO_2H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (i)$$

or

$$Me_2C{:}CHMe + Co^{3+} \longrightarrow CH_2{:}CMe{\cdot}CH{:}CH_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (ii)$$

$$CH_2{:}CMe{\cdot}CH{:}CH_2 + Co^{3+} \longrightarrow H{\cdot}CHO + H{\cdot}CO_2H + \text{other products in small amounts} \quad . \quad (iii)$$

The concentration of isoprene in solution increased to a stationary value determined by the condition that the rate of production equals the rate of oxidation of isoprene. Since

TABLE 4. *2-Methylbut-2-ene.*

Series :	1	2	3	4	5
Reaction conditions	Continuous shaking until complete reduction of Co^{3+}				Distillation of product prior to complete reduction
Vol. and concn. of $Co_2(SO_4)_3$ taken originally	153 ml. of 0·169N	258 ml. of 0·176N	163 ml. of 0·032N	1150 ml. of 0·016N	96 ml. of 0·136N
∴ Co^{3+} (g.-ions) taken	0·0259	0·0459	0·00523	0·0186	0·013
2-Methylbut-2-ene (moles) consumed	0·0127	0·0192	0·0019	0·0079	0·0029
Ratio of Co^{3+} reduced to olefin consumed	2·01	2·36	2·75	2·35	4·46
Ratio of acetone produced to olefin consumed	0·271	0·29	0·40	—	0·55
Ratio of carboxylic acid produced to olefin consumed	0·315	0·35	0·396	0·51	0·57
Ratio of acetaldehyde produced to olefin consumed	0·024	0·040	0·036	0·080	trace
Ratio of formaldehyde produced to olefin consumed	0·0008	0·0008	0·0004	0·0011	,,
Ratio of diene produced to olefin consumed	0·00138	0·00133	0·00835	0·0202	negligible
Diene concn. in product (M)	0·00012	0·000098	0·000093	0·00014	,,
Formic acid in carboxylic acid (%)	13·9	16·0	17·3	7·0	15·1
Ratio of Co^{3+} reduced to Co^{3+} reqd. to yield product	0·875	1·02	0·99	—	1·20

the concentration of the 2-methylbut-2-ene was fixed at its saturation limit the amount of isoprene in solution should be proportional to the total volume of the solution and this is in

[8] Milton and Waters, "Quantitative Microanalysis," Arnold, London, 1949, p. 124.

agreement with the results of series 1—4, Table 4. In series 5 the shaking was stopped before the cobaltic sulphate had been consumed. Under these conditions the 2-methylbut-2-ene in solution is rapidly consumed and thus the rate of isoprene formation decreased whilst any isoprene in solution is further oxidised. The stationary concentration of isoprene therefore rapidly falls to zero as observed experimentally.

The relative amounts of formic acid and acetic acid (or acetone) in the products (Table 4) show that approximately 8% of the 2-methylbut-2-ene is oxidised *via* isoprene. The analytical results may be expressed as

$$1{\cdot}00\ \text{2-Methylbut-2-ene} + 2{\cdot}01\ Co^{3+} \longrightarrow 0{\cdot}271\ \text{Acetone} + 0{\cdot}315\ \text{Acetic acid} + 0{\cdot}021\ \text{Acetaldehyde}$$
$$0{\cdot}00138\ \text{Isoprene} \longrightarrow 0{\cdot}051\ \text{Formic acid} + 0{\cdot}0008\ \text{Formaldehyde}$$

Calculation of the amount of cobaltic ion required to oxidise 2-methylbut-2-ene to these products gives the value of 2·30, compared with the average experimental value of 2·01. The agreement is satisfactory and it may be concluded that all the main products of the oxidation have been characterised and estimated. The detailed mechanism of the reaction will be discussed later in this paper.

2-Ethylbut-1-ene. The oxidation products in dilute sulphuric acid were determined in the same manner as those from 2-methylbut-2-ene; the main ones were formic acid and diethyl ketone. No diene was formed. Summation of the products gave the stoicheiometric relation

$$3{\cdot}34\ \text{2-Ethylbutene} + 9{\cdot}3\ Co^{3+} \longrightarrow 1{\cdot}38\ \text{Formic acid} + 1{\cdot}42\ \text{Diethyl ketone} + \text{unchanged 2-ethylbutene}$$

showing that the reaction occurred mainly by the rupture of the double bond to yield the two products isolated.

Pent-2-ene. The analyses from three experiments summarised in Table 5 show that the course of the oxidation is very similar to that of 2-methylbut-2-ene. The main reaction is the rupture of the olefin double bond to give aldehydes which are rapidly oxidised to acids while a secondary reaction leads to diene formation. The diene formed was not completely characterised but was most probably penta-1 : 3-diene. As in the case of 2-methylbut-2-ene the concentration of the diene reaches a stationary value when its rate of formation is equal to its rate of loss by oxidation and therefore

$$k_1F[Co^{3+}][\text{pent-2-ene}] = k_2[Co^{3+}][\text{diene}]$$

where F is the fraction of the pent-2-ene which is oxidised *via* the diene and k_2 is the bimolecular rate constant for the oxidation by cobaltic sulphate. The latter value has not been measured and so in deriving F from the above equation the corresponding value of k_2 for isoprene was used. The value of F so derived indicated that 14—15% of the hydrocarbon was oxidised *via* the diene. This should give a percentage yield of formic acid of 7·3%. The agreement with the experimental values (Table 5) of 6·9, 8·0, and 8·1% is somewhat fortuitous in view of

TABLE 5. *Pent-2-ene.*

Reaction conditions	Continuous shaking until all Co^{3+} reduced		
Vol. and concn. of $Co_2(SO_4)_3$ taken originally	163 ml. of 0·15N	2400 ml. of 0·0095N	180 ml. of 0·014N
∴ Co^{3+} (g.-ions) taken	$2{\cdot}35 \times 10^{-2}$	$2{\cdot}28 \times 10^{-2}$	$2{\cdot}5 \times 10^{-3}$
Vol. of pent-2-ene (ml.) consumed	1·5	0·98	0·148
Pent-2-ene (moles) consumed	$1{\cdot}5 \times 10^{-2}$	$9{\cdot}8 \times 10^{-3}$	$1{\cdot}48 \times 10^{-3}$
Ratio of Co^{3+} reduced to pent-2-ene consumed	1·57	2·32	1·69
Ratio of carboxylic acids produced to pent-2-ene consumed	0·352	0·60	0·41
Formic acid in carboxylic acid (%)	8·1	8·0	6·9
Ratio of formaldehyde produced to pent-2-ene consumed	$1{\cdot}3 \times 10^{-4}$	—	—
Ratio of other aldehydes produced to pent-2-ene consumed	$1{\cdot}1 \times 10^{-2}$	—	—
Diene concn. in product (M)	2·9	1·03	2·0
Ratio of diene produced to pent-2-ene consumed	$1{\cdot}31 \times 10^{-4}$	$1{\cdot}05 \times 10^{-2}$	$1{\cdot}01 \times 10^{-2}$
Absorption max. (mμ)	225	224	224
Calculated ratio of Co^{3+} reduced to pent-2-ene consumed	1·41	2·40	1·64
Ratio of Co^{3+} reduced to Co^{3+} reqd. to yield products	1·11	0·97	1·03

the approximations employed. However, the result does show that the formation of diene and its further oxidation can be treated quantitatively.

The results of the three analyses show that the mechanism of oxidation is

$$\text{Et·CH:CHMe} + Co^{3+} \xrightarrow{86\%} \text{Et·CHO} + \text{Me·CHO} \longrightarrow \text{Et·CO}_2\text{H} + \text{MeCO}_2\text{H}$$

$$\text{Me·CH:CH·CH:CH}_2 \xrightarrow{14\%} \text{H·CO}_2\text{H} + \text{other products}$$

Oct-1-ene. Oxidation showed that reaction occurred at the double bond to give formic acid and heptanoic acid. No diene or ketone was formed, indicating the absence of secondary mechanisms :

$$\text{C}_6\text{H}_{13}\text{·CH=CH}_2 + Co^{3+} \longrightarrow \text{C}_6\text{H}_{13}\text{·CO}_2\text{H} + \text{H·CO}_2\text{H}$$

Summary of Product Analyses.—All the results show that oxidation of the olefins with terminal double bonds by cobaltic sulphate splits the olefin at the double bond to give saturated aldehydes, which are rapidly oxidised to acids. With olefins in which the double bond is not in the terminal position, oxidative disruption of the olefin at the double bond is the

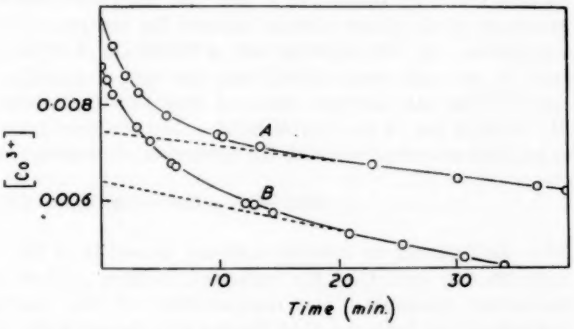


FIG. 5. *Rate of change of cobaltic ion concentration.*

main reaction, but a small fraction of olefin is oxidised to the diene by a secondary mechanism. The diene is itself oxidised by cobaltic sulphate, oxidative disruption again occurring at the double bonds.

When one of the doubly bonded carbon atoms is dialkyl-substituted, one of the main products formed on disruption of the double bond is a ketone. The ketone formed was relatively stable to cobaltic sulphate and was not further oxidised in the presence of excess of olefin.

Stoicheiometry.—The stoicheiometric ratio of cobaltic ion to 2-methylbut-2-ene reacting was determined by carrying out the reaction in the presence of an excess of cobaltic ion. Measurements of the change of cobaltic-ion concentration by light absorption showed that the rate of reduction to Co^{2+} was initially rapid, becoming slow when 4—5 cobaltic ions per molecule of 2-methylbut-2-ene had been reduced. Typical plots of the change of cobaltic ion concentration with time are shown in Fig. 5. The amount of cobaltic sulphate reduced in the initial fast reaction was determined by extrapolation of the slow reaction to zero time as indicated by the broken line. The values for the stoicheiometric ratio (Table 6) show that 4—5 equivalents of

TABLE 6.

Run	$10^3 \times$ Concn. of 2-methylbut-2-ene (M)	$10^3 \times$ Concn. of cobaltic ion used (g.-ion/l.)	Stoiocheiometric ratio Co^{3+}/2 methylbut-2-ene
41	0·33	1·77	5·36
42	0·66	2·80	4·24
43	0·40	2·17	5·43

Co^{3+} are consumed per molecule of olefin in the faster reaction. The slower reaction corresponds to the further oxidation of the initial products and the significance of these results will be discussed later.

Discussion

The kinetics of the acid-catalysed hydration of olefins in aqueous solution have been studied by Lucas and his co-workers [9] who showed that the effective catalyst was the hydroxonium ion. The addition occurs by the two-stage process

$$R{\cdot}CH{=}CH_2 + H{\cdot}OH_2^+ \longrightarrow R{\cdot}\overset{+}{C}H{-}CH_3 + OH_2$$
$$R{\cdot}\overset{+}{C}H{-}CH_3 + OH_2 \longrightarrow R(CH{\cdot}OH_2^+){\cdot}CH_3$$

The evidence now summarised indicates that this is not the primary step in the reaction of the olefins with cobaltic ions: (1) The reaction in all cases was found to be independent of the hydrogen-ion concentration, which is not in agreement with the possibility of the olefin's reacting as an alkoxonium ion. A study of the kinetics of the oxidation of *tert.*-amyl alcohol by cobaltic ion (the product of the hydration of 2-methylbut-2-ene) showed that the rate depended very markedly on the hydrogen-ion concentration and was similar to that found by Bawn and White [2] for the lower primary alcohols. (2) The absorption spectrum of the olefin solution showed the absence of hydration under the experimental conditions. (3) The reported rate of hydration of olefins under similar conditions to those used by us were much slower than the rate of oxidation by cobaltic sulphate. (4) The second-order rate kinetics observed show that the initiation reaction is a direct attack of the cobaltic ion at the double bond. The evidence presented indicates that this reaction is an electron extraction with the formation of a reactive radical ion, *viz.*:

$$R{\cdot}CH{=}CH_2 + Co^{3+} \longrightarrow R{\cdot}\dot{C}H{-}\overset{+}{C}H_2 + Co^{2+}$$

The small change in velocity constant caused by a 20-fold change in ionic strength also supports the view that the measured reaction is that between the cobaltic ion and an uncharged molecule. The independence of the reaction rate on hydrogen-ion concentration also indicates that the reactive species is the hydrated cobaltic ion rather than the ion pair $(Co,OH)^{2+}$. It would be expected that the rate of oxidation by $(Co,OH)^{2+}$ would be slower than that by Co^{3+} and in the oxidation of benzene by cobaltic perchlorate Baxendale and Wells [10] observed that the activation energy of the ion-pair reaction was 17 kcal. greater than that of the hydrated ion. Both the last reactions were, however, measurable owing to the favourable entropy of activation of the ion-pair reaction.

Energetics of Primary Process.—The heat of the reaction

$$(RHC{=}CH_2)_{aq} + Co^{3+} \longrightarrow (RH\overset{+}{C}{-}\dot{C}H_2)_{aq} + Co^{2+}{}_{aq} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

can be calculated from the energy of ionisation of cobaltous ion and ΔH_1 as determined by the following cycle:

$$\begin{array}{ccc} (RHC{=}CH_2)_g & \xrightarrow{I_0} & (RH\overset{+}{C}{-}\dot{C}H_2)_g + e \\ \uparrow Q_0 & & \downarrow Q_0{}^+ \\ Co^{3+} + (RHC{=}CH_2)_{aq} & \xrightarrow{\Delta H_1} & (RH\overset{+}{C}{-}\dot{C}H_2)_{aq} + Co^{2+} \end{array}$$

where I_0 is the ionisation potential of the olefin, and Q_0 and $Q_0{}^+$ are the heat of solution of olefin and radical ion respectively. $Q_0{}^+$ has not been measured and was assumed to be equal to the heat of hydration of the carbonium ion Me_2CH^+, *ca.* 74 kcal.[12] $I_0 =$ 220·2 kcal. for monoalkyl olefins and Q_0 was taken as approximately equal to the latent

[9] Lucas and Liu, *J. Amer. Chem. Soc.*, 1934, **56**, 2138; Lucas and Eberz, 1934, **56**, 460.
[10] Baxendale and Wells, *Discuss. Faraday Soc.*, 1953, **14**, 239.

heat of vaporisation (= 5·0 kcal.). The ionisation potential of the cobaltous ion in aqueous solution (J) can be derived from the following reaction :

$$Co^{2+}_{aq} + H^{+}_{aq} \xrightarrow{\Delta H_2} Co^{3+}_{aq} + \tfrac{1}{2}(H_2)_{aq}$$

$$J = \Delta H_2 + \tfrac{1}{2}D(H_2) + I(H) - Q(H^+)$$

where $D(H_2)$ is the dissociation energy of hydrogen and $Q(H^+)$ is the heat of solution of the proton. The free energy of the cobaltous–cobaltic change referred to the hydrogen electrode is 42·5 cal. and ΔH_2 can be determined from $\Delta H = \Delta G - T\Delta S$ by use of the entropy relation :

$$S_2 = S(Co^{3+}) + \tfrac{1}{2}S(H_2) - S(Co^{2+}) - S(H^+)$$

Now $S(Co^{2+}) = -27$, $\frac{1}{2}S(H_2) = 15{\cdot}6$, $S(H^+) = 0$, and $S(Co^{3+}) = -71{\cdot}8$ e.u. and hence $S_2 = -29{\cdot}2$ e.u. The entropy of the cobaltic ion was estimated by comparison with the entropies and ionic radii of Cr^{3+} and Fe^{3+} :

Ion	Ionic radius (Å)	Entropy in aqueous soln. at 25°
Cr^{3+}	0·62	−73·5
Co^{3+}	0·63	—
Fe^{3+}	0·64	−70·1

Hence $\Delta H_2 = 33{\cdot}8$ kcal. and the ionisation potential of the cobaltous ion in solution is 117·3 kcal., as obtained from the above equation by using $D(H_2) = 104{\cdot}1$, $I(H) = 313{\cdot}4$, and $Q(H^+) = 282$ kcal., respectively. The endothermicity of the electron abstraction from a monoalkyl-olefin by the cobaltic ion is given by

$$\Delta H = \Delta H_1 - J = Q_0 + I_0 - Q_0{}^+ - J = 33{\cdot}9 \text{ kcal.}$$

A similar calculation of the endothermicity of the reaction $(Me_2C{=}CHMe)_{aq} + Co^{3+}_{aq} \longrightarrow (Me_2\overset{+}{C}{-}\dot{C}HMe)_{aq} + Co^{2+}_{aq}$ gave a value of 21·6 kcals. The heat of solution of the radical ion was assumed to be that of Me_3C^+ (= 69·0 kcal.) and the ionisation potential of trimethylethylene according to Honig [11] is 17·3 kcal. less than that of the monosubstituted ethylene. Within the limits of the accuracy of the thermochemical data the endothermicities approximate closely to the observed activation energies of 29 and 27 kcal. respectively. On energetic grounds therefore it may be concluded that reaction (1) is probable.

Effect of Substitution on Olefin Reactivity.—Comparison of the bimolecular rate constants at 25° shows that trialkylolefins react about 6 times as fast as the monoalkylethylenes and that dialkylethylenes react 2—3 times as fast as the monoalkyl derivatives. Although E (Table 3) cannot be measured with the same accuracy as the rate constant the result shows that the effect of substitution largely affects the activation energy and not the frequency factor. These results may be understood in terms of the energy of the transformation

$$(R{\cdot}CH{=}CH_2)_{aq} \longrightarrow (R{\cdot}\overset{+}{C}H{-}\dot{C}H_2)_{aq} + e \quad \ldots\ldots\ldots \quad (2)$$

since the $Co^{3+}_{aq} \longrightarrow Co^{2+}_{aq}$ reaction contributes a constant energy term independent of the olefin. The endothermicity of eqn. (2) is given by $\Delta H_2 = S_i{}^+ - S_i - I$ where $(S_i{}^+ - S_i)$ is the difference of solvation energies of the ion-radical and the olefin and I is the ionisation potential of the olefin. We make the reasonable assumption that $S_i{}^+$

[11] Honig, *J. Chem. Phys.*, 1948, **16**, 105.
[12] Evans, *Trans. Faraday Soc.*, 1946, **42**, 722.

depends on the number of groups attached directly to the positive carbon atom and that substitution farther away has a negligible effect. For the change from a secondary to a tertiary ion Evans [12] showed that $(S_t^+ - S_i)$ was approximately -5 kcal. The ionisation potentials of the olefins and styrene as measured by electron-impact and spectrosopic data are summarised in Table 7 together with the values of ΔH_2.

TABLE 7.

	Ionisation potential			
	Electron impact	Spectroscopic	$\Delta(S_t^+ - S_i)$	ΔH_2
2-Methylbut-2-ene	—	8·75	−0·22	−8·98
Pent-2-ene	9·16	9·16	0	−9·16
2-Ethylbut-1-ene	—	—	0	—
Hex-1-ene	9·59	—	0	−9·59
Hept-1-ene	9·54	—	0	−9·52
Oct-1-ene	9·52	—	0	−9·52
Styrene	8·82	8·81	0	−8·81
Isoprene	9·08	—	0	−9·08

Since the configuration of the transition state will be similar for all the olefins it is to be expected that variation of the energy of activation ΔE with change of substituent attached to the double bond will be related to the endothermicity of the reactions. This conclusion is in agreement with the estimated changes in ΔH_2 for the three cases in which the energy of activation was measured. Moreover, since the main influence of the substitutent is reflected in the change of ΔE and not the entropy of activation ΔS^*, it is justifiable to compare ΔH_2 with changes in the measured rate of reaction. This shows very clearly that changes in k follow closely those in ΔH_2, and the results indicate a relationship between ΔE and ΔH of the form $\Delta E = \alpha \Delta H$ as observed with other systems in which the structure of one of the reactants has been varied.

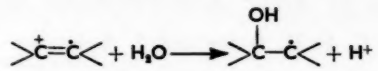
Parallel effects of substituents in influencing reactivity seem to be characteristic of the reaction of olefins with positive groups and similar results have been observed in measurements of the rate of bromination,[13] acid-catalysed hydration,[14] oxidation by peracetic acid,[15] and in the ionic polymerisation of olefins.[16]

The very high values of the entropy of activation of about 30 e.u. are much greater than usually observed in the reaction between an ion and a neutral molecule, and correspond to a considerable increase in the degrees of freedom of the reaction system. Although the combination of an olefin molecule and a cobaltic ion to form the activated complex occurs with a decrease in translational degrees of freedom of the reactants there will be a considerable increase in the degrees of freedom of the water molecules released from the hydration shell of the cobaltic ion. In the transition complex the charge will be distributed on the olefin and the metal ion. The olefin can be regarded as breaking up the symmetry of the hydration shell by displacing some of the water molecules in forming the complex. This large increase in entropy also supports the view that the hydrated cobaltic ion (entropy = −71·3 e.u.) is the reactive species rather than the ion-pair $(Co,OH)^{2+}$ (entropy estimated by analogy with $FeOH^+$ to be −24·0 e.u.) since reactions between ions and molecules usually involve small entropy changes and the increase in entropy is greater for reactions of an ion which has the more negative entropy.

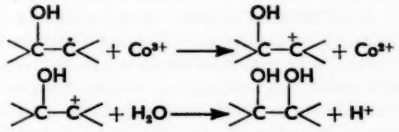
Secondary Oxidation Reactions.—The main course of the oxidation to give the observed products—ketones, aldehydes, acids, etc.—must result from the disruption of the double bond and this occurs by a series of reactions in which the carbonium ion reacts with water to give hydroxylic compounds which are then rapidly oxidised by the cobaltic ion in

[12] Anantakrishnan and Ingold, *J.*, 1935, 984.
[14] Lucas and co-workers, *J. Amer. Chem. Soc.*, 1934, **56**, 2138; Lucas and Eberz, 1934, **56**, 460.
[15] Swern, *Chem. Rev.*, 1949, **45**, 48.
[16] Norris and Halpern, *J. Amer. Chem. Soc.*, 1927, **49**, 873.

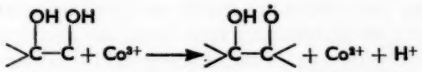
successive stages until relatively stable products are formed. Thus, after the rate-determining reaction (1), the radical ion reacts with the aqueous solvent according to



The radical formed is stable to water but reacts rapidly with Co^{3+}, since the ionisation potential of this type of radical (6·5—7·6 e.v.) is very much lower than that of the initial olefin (8·8—9·7 e.v.), to give a carbonium ion which on further reaction with water gives a glycol :

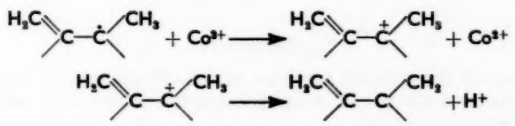


Glycols are readily oxidised by cobaltic salts and glycol fission ensues by a one-electron transfer with the formation of a free radical as in the above reactions, *viz.*,



The radical so formed rapidly disrupts into an aldehyde R·CHO or ketone RR'CO and the radical $>\dot{C}-OH$. The last, by further reaction with Co^{3+}, again gives an aldehyde or ketone. A similar reaction scheme has been postulated by Drummond and Waters [17] and by Duke and his co-workers [18] for the oxidation of pinacol by manganic and ceric salts respectively. The aldehydes formed in these secondary reactions are further oxidised by a similar series of successive single-electron transfer and hydroxylation steps to yield carboxylic acids. This reaction scheme consisting of a series of simple electron-transfer processes of the cobaltic ion not only explains the formation of the products but is in agreement with the observed stoicheiometry of the overall oxidation.

The small amount of diene in the final product indicates that the radical ion $>\overset{+}{C}-\dot{C}<$ can lose a proton to yield a resonance-stabilised allylic radical. The latter is oxidised by Co^{3+} to a carbonium ion which splits off a hydrogen ion to form the diene, for example



The absence of diene in the oxidation of olefins having terminal double bonds is in conformity with these views.

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DEPARTMENT OF INORGANIC AND PHYSICAL CHEMISTRY,
THE UNIVERSITY, LIVERPOOL. [*Received, October 12th*, 1956.]

[17] Drummond and Waters, *J.*, 1953, 435.
[18] Duke and Bremer, *J. Amer. Chem. Soc.*, 1951, **73**, 5179; Duke and Forist, *ibid.*, 1947, **69**, 2790.

352. *Reactions of the Cobaltic Ion. Part V.* Oxidation of Olefins by Cobaltic Salts in Acetic Acid–Sulphuric Acid Mixtures.*

C. E. H. Bawn and J. A. Sharp.

In contrast to the oxidation of olefins by cobaltic salts dissolved in dilute sulphuric acid, similar olefins are not oxidised by a cobaltic acetate solution in glacial acetic acid. We have measured the rate of oxidation of 2-methylbut-2-ene, oct-1-ene, and 2 : 4 : 4-trimethylpent-2-ene in mixed acetic–sulphuric acids. The rate of reaction depends on the solvent used for the cobaltic salt. With cobaltic sulphate initially dissolved in sulphuric acid and the olefin in glacial acetic the second-order reaction between Co^{3+} and the olefin agrees very closely with measurements in dilute sulphuric acid (Part IV*). On the other hand, the oxidation of olefins dissolved in acetic acid by cobaltic sulphate dissolved in acetic acid–sulphuric acid obeys a first-order relation for the rate of reduction of the cobaltic complex, independent of the olefin concentration. The drastic change in kinetics is interpreted as being due to the formation of a stable complex cobaltic sulphate–acetate ion.

In Part IV* it was shown that olefins are readily oxidised by solutions of cobaltic salts in dilute sulphuric acid, the rate-determining step being the abstraction of an electron from the double bond by the cobaltic ion. Glacial acetic acid is commonly used as solvent for non-aqueous oxidations and, in contrast with the previous results in aqueous acid, it is observed that neither the straight-chain nor the branched olefins were oxidised by cobaltic acetate in this solvent. Solutions of the olefins in glacial acetic acid containing cobaltic acetate (prepared both by electrolytic oxidation and by dissolution of dry cobaltic sulphate in acetic acid) showed no change in absorption over several days. It is shown in Part VI (in the press) that cobaltic acetate dissolved in glacial acetic acid decomposes hydroperoxides and that the cobaltic complex in acetic–sulphuric acid mixtures is a much stronger oxidising agent than cobaltic acetate alone. We now report measurements of the oxidation of olefins in mixed acids; it is observed that the cobaltic complex formed by the addition of the cobaltic salt to acetic acid containing added sulphuric acid oxidised the olefin more slowly than in sulphuric acid alone. The rate of reduction of the cobaltic complex by the olefin also obeyed a different kinetic relation from that found with aqueous sulphuric acid solution although the products of the reactions were unaltered.

Experimental

The transformation of the cobaltic complex to the cobaltous state was followed by light-absorption measurements with the Unicam spectrophotometer and temperature-controlled cell described in the preceding paper.

The solution of the oxidising agent in acetic–sulphuric acid mixtures was prepared by adding the cobaltic sulphate solution in sulphuric acid to glacial acetic acid before the commencement of measurement. The olefin was dissolved in glacial acetic acid.

I. *Oxidation of Olefins dissolved in Glacial Acetic Acid by Cobaltic Sulphate Solution in Acetic Acid–Sulphuric Acid.—2-Methylbut-2-ene.* The rate of change of cobaltic into cobaltous ion was of the first order with respect to the cobaltic complex concentration as is shown by a series of typical plots given in Fig. 1 (a = initial molar concentration of cobaltic ion). Variation of the olefin concentration over a very wide range with all other variables of concentration fixed had no marked influence on the rate of reduction of the cobaltic complex as shown by the summarised results of Table 1. A similar series of rate measurements carried out for a range of sulphuric and acetic acid concentrations also summarised in Table 1 show that the composition of the acid mixture, and thus the hydrogen-ion concentration, had no influence on the rate of reaction. The value of the first-order constants ($k_{obs.} = -\mathrm{d} \log_{10} x/\mathrm{d}t$) for the region in which cobaltic concentration is similar to or less than that of the olefin could not be measured very

* Part IV, preceding paper.

accurately since the concentration of the olefin decreased appreciably during the course of the reaction. However, even these results demonstrated the small effect of change of the initial olefin concentration.

The effect of temperature on the rate of oxidation of 2-methylbut-2-ene was measured for the solution of composition acetic acid 14·8N, sulphuric acid 1·33N, and olefin 0·0125M. The logarithms of the observed first-order constants plotted against the reciprocal of the temperature were linear and the slope corresponds to an activation energy for the reaction of 30·8 kcal./mole.

Oct-1-ene and 2 : 4 : 4-trimethylpent-2-ene. Measurements with these hydrocarbons were carried out as with 2-methylbut-2-ene. The rate of cobaltic-ion consumption was of the first order with both olefins and, as shown by the results presented in Tables 2 and 3, the rate of

TABLE 1. *Oxidation of 2-methylbut-2-ene dissolved in glacial acetic acid by cobaltic sulphate dissolved in acetic acid–sulphuric acid mixtures.*

$a = 1·92 \times 10^{-4}$M. Temp. = 24·9°.

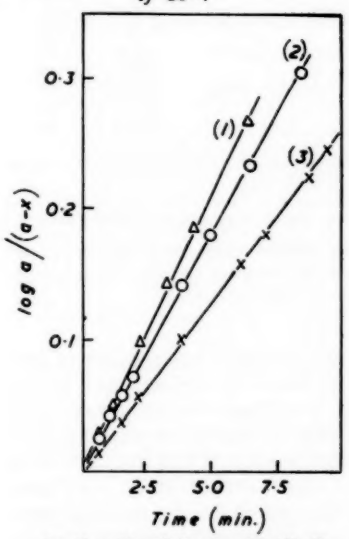
$Me·CO_2H$ (M)	H_2SO_4 (N)	Olefin (M)	$k_{obs.}$ (min.$^{-1}$)
14·9	1·25	0·480	0·0362
		0·0283	0·0240
		0·00085	0·0180
13·0	2·1	0·00282	0·020
		0·00048	0·026
		0·00028	0·0229
16·3	0·42	0·302	0·0422
		0·047	0·0265
		0·0094	0·0339

TABLE 2. *Oxidation of oct-1-ene by cobaltic complex in acetic acid–sulphuric acid mixture.*

$a = 1·92 \times 10^{-4}$M.

$Me·CO_2H$ (M)	H_2SO_4 (N)	Olefin (M)	$k_{obs.}$ (min.$^{-1}$)	Temp.
16·3	0·42	0·0554	0·0213	22·0°
		0·0111	0·0162	
		0·277	0·0144	
14·2	1·66	0·0221	0·0145 *	
			0·0163 *	
			0·0120 †	20·0
			0·0116 †	

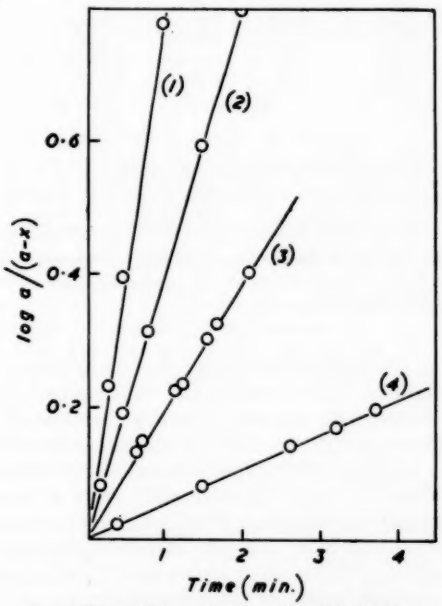
FIG. 1. *First-order plot of the reduction of* Co^{3+}.



Acetic acid–sulphuric acid: **(1, 3)** 16·3M–0·42M; curve (2) 14·9M–1·25M. $a = 1·92 \times 10^{-4}$M.

Concn. of 2-methylbut-2-ene: (1) 0·302M; (2) 0·48M; (3) 0·047M.

FIG. 2. *First-order plots of the reduction of* Co^{3+} *by 2-methylbut-2-ene.*



$a = 1·92 \times 10^{-4}$M. Concn. of 2-methylbut-2-ene: (1) $1·44 \times 10^{-2}$M; (2) $0·72 \times 10^{-2}$M; (3) $0·36 \times 10^{-2}$M; (4) $0·12 \times 10^{-2}$M. Temp. = 20·4°.

reaction was only slightly dependent on olefin concentration. Hence the kinetic relations are similar for the three hydrocarbons and the rate constants are also of similar magnitude. The rate of reduction of the cobaltic complex by hex-1-ene and hept-1-ene could not be measured by the light-absorption method since the addition of sulphuric acid to solutions of these olefins in glacial acetic acid produced deep green and blue colours, respectively. That these coloured compounds, which may be addition complexes between the olefins and sulphuric acid, have no influence on the rate of oxidation of the olefin was shown by measurements of rates of reactions in which all reactant concentrations were kept constant and (*a*) the sulphuric acid was added to the solution of olefin in acetic acid several hours before addition of the cobaltic compound or (*b*) the cobaltic ion in the required concentrations of sulphuric and acetic acids was added to the olefin in glacial acetic acid. Two such pairs of experiments with oct-1-ene are denoted by * and † in Table 2 and it may be concluded that addition-compound formation of the olefin and sulphuric acid did not affect the rate of oxidation.

Products of Oxidation.—The products of the oxidation of 2-methylbut-2-ene by the cobalt complex formed in 90% acetic acid–10% 10N-sulphuric acid were analysed by the methods described in Part IV. The reactants formed a homogeneous solution and reduction of the cobaltic state was complete within 1 hr. The average analysis from several experiments, excluding acids which were difficult to separate from acetic acid, was

9·5 2-Methylbut-2-ene + 20 Co^{3+} ⟶ 3·12 carbonyl group (mainly acetone) + 0·04 diene

In spite of the marked change in kinetic relations these results show that the type and relative distribution of the products were very similar to those observed in aqueous sulphuric acid (Part IV).

TABLE 3. *Oxidation of 2 : 4 : 4-trimethylpent-2-ene by cobaltic complex in acetic acid–sulphuric acid mixture.*

$a = 1·92 \times 10^{-4}$M. Temp. = 22·0°.

Me·CO_2H (M)	H_2SO_4 (N)	Olefin (M)	$k_{obs.}$ (min.$^{-1}$)
16·3	0·42	0·0111	0·0126
14·9	1·25	0·0332	0·0157
16·3	0·42	0·0554	0·0146
16·3	0·42	0·277	0·0227

TABLE 4. *Oxidation of 2-methylbut-2-ene in acetic acid–sulphuric acid mixtures.*

Temp. = 20·4°. $a = 1·92 \times 10^{-4}$M.

Me·CO_2H (M)	H_2SO_4 (N)	Olefin (100 × M)	$k_{obs.}$ (min.$^{-1}$)	$k_{obs.}$/[olefin]
8·5	5·0	1·44	0·74	51
			0·78	54
		0·72	0·404	56
			0·378	53
		0·36	0·191	53
			0·197	55
		0·12	0·055	46

DISCUSSION

The first-order relation for the reduction of the cobaltic complex independent of acid and olefin concentration can be explained by either of the following mechanisms. (1) An intermediate complex is formed between the olefin and the cobaltic salt, the first-order decomposition of which is the rate-determining step. This mechanism is unlikely since it would require immediate and fairly complete complex-formation of the reactants even when the metal ion and olefin were at approximately equal concentration. We have sought the formation of such a complex with cobaltic salts without finding any indication of its existence. (2) The first-order dissociation of the cobaltic acetate complex gives an active cobaltic ion complex which reacts rapidly with the olefin. The rate-determining step here would be the dissociation process which could be imagined to occur by an S_N1 type of mechanism as observed with six other substitution reactions of complex cobalt salts.[1] Although the precise structures cannot as yet be formulated the process may be pictured broadly as

$$\text{Cobaltic acetate complex} \xrightarrow[\text{slow}]{} \text{Active cobaltic complex} \xrightarrow[\text{fast}]{\text{olefin}} Co^{2+} + \text{Products}$$

II. *Oxidation of 2-Methylbut-2-ene dissolved in Acetic Acid by Cobaltic Sulphate dissolved in Sulphuric Acid.*—When a solution of cobaltic sulphate dissolved in 10N-sulphuric acid instead

[1] Ingold, "Kinetics and Mechanism of Inorganic Reactions in Solution," *Chem. Soc. Special Publ. No.* 1, 1954, p. 10.

of acetic–sulphuric acid mixtures was added to an equal volume of a solution of 2-methylbut-2-ene in glacial acetic acid, the rate of reduction of the cobaltic compound was of the first order with respect to the cobaltic-ion concentration as before, as shown by the first-order plot in Fig. 2, and was now also of the first order with respect to the olefin concentration (Table 4). At 20·4° the kinetic relation

$$-d[Co^{3+}]/dt = 2{\cdot}0[Co^{3+}][\text{2-methylbut-2-ene}] \text{ (moles l.}^{-1}\text{ sec.}^{-1}\text{)}$$

was obeyed. This bimolecular rate expression was in very close agreement with that obtained (Part IV) for the oxidation of 2-methylbut-2-ene by cobaltic sulphate in dilute sulphuric acid. Hence under the above experimental conditions the cobaltic ion reacts in the same way as in dilute sulphuric acid solution and is therefore reacting with the olefin before conversion into the more stable cobaltic sulphate–acetate complex. These results indicate that the drastic change in the rate and the kinetic relationships on dissolving cobaltic sulphate in an acetic acid–sulphuric acid mixture is caused by complex-formation of the cobaltic ion and that the reactivity of the olefin is not changed by previous dissolution in acetic acid.

DEPARTMENT OF INORGANIC AND PHYSICAL CHEMISTRY,
THE UNIVERSITY, LIVERPOOL. [*Received, October 12th*, 1956.]

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353. *The Configuration of the Ribitol Phosphate Residue in Cytidine Diphosphate Ribitol.*

By J. BADDILEY, J. G. BUCHANAN, and B. CARSS.

The ribitol cyclic phosphate (IV), obtained from cytidine diphosphate ribitol (CDP-ribitol) and hot ammonia, was oxidised with periodate and then bromine water to glyceric acid 2 : 3-(hydrogen phosphate) (V). On brief acid treatment this yielded a mixture (probably) of glyceric acid 2- and 3-phosphates (VI and VII), the configuration of which was determined with a mixed enzyme system from rabbit muscle where D-glyceric acid phosphates are known metabolites.

The ribitol cyclic phosphate from CDP-ribitol, like that from D-ribitol-5 phosphate, gave a product fully active in the enzyme system, whereas the L-isomer was inactive. It is concluded that the nucleotide contains a D-ribitol-5 phosphate residue. The biochemical significance of this is discussed.

The isomeric ribitol phosphates formed during acid-catalysed racemisation of the 5-phosphate have been identified.

The glycerophosphate residue in cytidine diphosphate glycerol has the L-configuration.

ONE of the nucleotides isolated from *Lactobacillus arabinosus* [1,2] has been shown [3] to be P^1-cytidine-5′ P^2-ribitol-1 pyrophosphate (I), conveniently called cytidine diphosphate ribitol (CDP-ribitol). Although ribitol is symmetrical, its 1-phosphate is not, and there remained the problem of establishing the configuration of this residue in CDP-ribitol. The isomerism in the 1-phosphates of ribitol is similar to that in the α-glycerophosphates.

For the related nucleotide, cytidine diphosphate glycerol, it has now been shown that the α-glycerophosphate, produced from the nucleotide by the action of a rattlesnake venom enzyme,[4] is readily and completely oxidised to dihydroxyacetone phosphate by the enzyme glycerophosphate dehydrogenase (experiments were kindly performed by

[1] Baddiley and Mathias, *J.*, 1954, 2723.
[2] Baddiley, Buchanan, Carss, Mathias, and Sanderson, *Biochem. J.*, 1956, **64**, 599.
[3] Baddiley, Buchanan, Carss, and Mathias, *J.*, 1956, 4583.
[4] Baddiley, Buchanan, Mathias, and Sanderson, *J.*, 1956, 4186.

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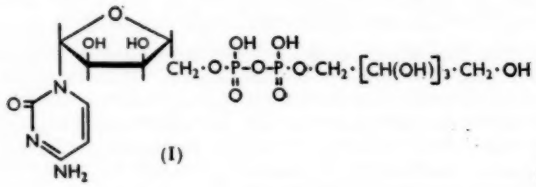
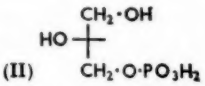
Dr. D. E. Hughes and Mr. A. R. Sanderson). This enzyme is specific in its action on L-α-glycerophosphate (II). It is concluded that the α-glycerophosphate residue in CDP-glycerol has the L-configuration. The observation is consistent with the fact that α-glycerophosphate from other natural sources has the L-configuration.[5]



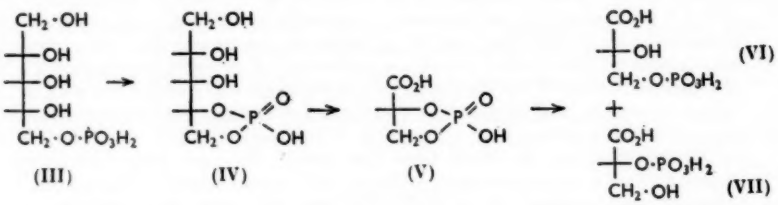
(I)



(II)

As in the case of the glycerol-containing nucleotide, very small amounts of CDP-ribitol were available, and it was considered unlikely that direct measurements of rotations on the ribitol phosphate derived from it would be possible by the conventional methods at our disposal. As ribitol phosphates had not been encountered hitherto in Nature no specific and direct enzymic method could be used for determining the configuration in the ribitol-containing nucleotide. A micromethod has now been developed for the degradation of ribitol-1 phosphates to glyceric acid phosphates and their subsequent determination by enzymic reactions. The degradation is outlined in the annexed formulæ.

D-Ribitol-1 phosphate (III),* prepared by reduction of D-ribose-5 phosphate with sodium borohydride, was cyclised to the 4 : 5-(hydrogen phosphate) (IV) through the action of trifluoroacetic anhydride.[3] A few milligrams were purified by paper chromatography; the material was eluted from the paper and oxidised with sodium metaperiodate, followed



(III) (IV) (V) (VI) (VII)

by bromine water. It is assumed that the periodate oxidation yields D-glyceraldehyde 2 : 3-(hydrogen phosphate), which is further oxidised by bromine to D-glyceric acid 2 : 3-(hydrogen phosphate) (V). Without isolation the cyclic phosphate was hydrolysed by brief treatment with Dowex-50 resin (H^+ form) and the resulting mixture of D-glyceric acid 3- (VI) and 2-phosphate (VII) was run on a paper chromatogram. It was important to demonstrate that no inorganic phosphates had been formed during the series of reactions. The proportion of the two glyceric acid phosphates in the mixture was unimportant (see below), but the ratio [6] of 3- to 2-isomer is probably about 4 : 1. The authenticity of the

* D-Ribitol 5-phosphate is, of course, the same substance as L-ribitol 1-phosphate. According to the standard rules of nomenclature, the name with the lower number should have preference, *i.e.*, L-ribitol 1-phosphate. Nevertheless, D-ribitol-5 phosphate is used in this paper because of its use in previous papers and because the substance is probably related metabolically to D-ribose 5-phosphate and D-ribulose 5-phosphate and is degraded to D-glyceric acid. Moreover, it was important to avoid the possible implication that L-ribitol 1-phosphate is in any way related to L-α-glycerophosphate. These two compounds are, in fact, in stereochemically opposite series. The correct name for the naturally occurring L-α-glycerophosphate (II), according to standard rules of nomenclature, is D-glycerol 1-phosphate (equivalent to L-glycerol 3-phosphate). However, probably for reasons concerning its biochemical origin, the L-α or L-3 nomenclature has always been adopted for this compound and we have retained it in this paper.

[5] Baer and Fischer, *J. Biol. Chem.*, 1939, **128**, 491.
[6] Ballou and Fischer, *J. Amer. Chem. Soc.*, 1954, **76**, 3188.

mixture was shown by enzymic dephosphorylation of a sample extracted from paper to give glyceric acid, identified by paper chromatography.

Both D-glyceric acid 2- and 3-phosphate are known intermediates in the alcoholic fermentation of glucose in yeast and in the conversion of glucose into lactic acid in muscle. It was thought that if the mixed phosphates obtained from the above degradation of D-ribitol-5 phosphate were added to a multi-enzyme system from yeast or muscle their incorporation into the glucose metabolic system would be measurable. A mixed enzyme preparation from rabbit muscle (kindly provided by Dr. G. R. Greenberg) was used in our experiments. Adenosine triphosphate (ATP) and magnesium ions were added to the enzyme solution and utilisation of glyceric acid phosphates was measured by the oxidation of reduced diphosphopyridine nucleotide (DPNH). The oxidation was observed spectrophotometrically by standard methods.[7]

When the above degradation and enzymic assay were carried out on D-ribitol-5 phosphate it was found that one mol. of DPNH was oxidised per mol. of glyceric acid phosphate (calculated as organic phosphate) added, and the same behaviour was observed with standard glyceric acid phosphate. The reaction products from this multi-enzyme system have not been identified, but it is probable that lactic acid is the principal one.

The nature of the products in the enzymic test and even the correct identity of the chemical degradation products are not important for our purposes, provided that the test can be shown to be specific for D-ribitol-5 phosphate. It was necessary then to show that L-ribitol-5 phosphate, after degradation, yielded products inactive in the enzymic assay. Pure L-ribitol-5 phosphate would be difficult to obtain, but the specificity of the test would be demonstrated if the DL-compound exhibited half of the activity of the D-5 isomer.

Racemisation of phosphates of symmetrical polyols is readily achieved by phosphate migration under acid conditions. In the studies leading to the structure of CDP-ribitol it was found that treatment of D-ribitol-5 phosphate with acid gave a mixture of phosphates, which were separable by paper chromatography.[3] The 1(5)-phosphate had the lowest R_P value of the phosphates in the *n*-propyl alcohol–ammonia solvent and could be isolated in pure form from chromatograms. Samples of D-ribitol-5 phosphate were treated with N-hydrochloric acid at 100° for different periods of time and the 1(5)-phosphate was re-isolated from a paper chromatogram. The degradation procedure and enzyme test were repeated and it was found (see Table 1) that in each case DPNH oxidation reached an end-point corresponding to less than one mol. per mol. of organic phosphate. This implied that the enzyme system was inactive with the L-glyceric acid phosphates, in confirmation of the work of Meyerhof and Kiessling.[8] The measurements indicated, moreover, that racemisation of the ribitol phosphates had been substantial after 30 minutes and was complete after 90 minutes. It followed that the test would be specific in determining the configuration of the ribitol phosphate from CDP-ribitol.

Ribitol 1 : 2-(hydrogen phosphate) can be obtained directly from CDP-ribitol by treatment with hot aqueous ammonia. A sample prepared in this way was isolated from a paper chromatogram, then degraded, and the products were tested by the enzymic method. One mol. of DPNH was oxidised for each mol. of organic phosphate (see Table 1) and it is concluded that the ribitol phosphate residue in CDP-ribitol corresponds to D-ribitol-5 phosphate.

The other phosphates produced by acid treatment of D-ribitol-5 phosphate have now been identified. The earlier work[3] had shown that, besides anhydroribitol and a phosphate with the same chromatographic properties as the original, two compounds were produced with R_P values slightly greater than that of ribitol-1(5) phosphate in *n*-propyl alcohol–ammonia. The unknown compound with the higher R_P value (" YS ") gave a yellow colour a few minutes after being sprayed with the periodate–Schiff reagents; that with the lower R_P value (" PS ") gave a purple colour with these reagents in the same way

[7] Colowick and Kaplan, " Methods in Enzymology," Vol. I, Academic Press, New York, 1955.
[8] Meyerhof and Kiessling, *Biochem. Z.*, 1935, **276**, 239.

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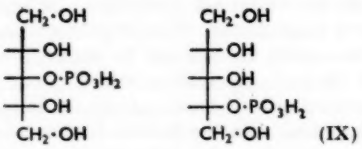
as did ribitol-1(5) phosphate. YS and PS could not be completely resolved and the experiments described below, which prove that YS is ribitol-3 phosphate (VIII) and PS is ribitol-2(4) phosphate (IX), were carried out on mixtures of the two.

TABLE 1. *Action of rabbit muscle enzymes on glyceric acid phosphates.*

Sample of glyceric acid phosphates (PGA)	PGA (mol.) (phosphate detn.)	D-PGA (mol.) (enzyme assay)	D-PGA (%) in mixture
A	0·50, 0·50	0·49, 0·50	98, 100
B	0·18, 0·18	0·13, 0·13	72, 72
C	0·58, 0·58	0·27, 0·28	47, 48
D	0·70, 0·69	0·33, 0·33	47, 48
E	0·53, 0·54	0·55, 0·55	104, 102

A, From D-ribitol-5 phosphate. B, From D-ribitol-5 phosphate, treated with acid for 30 min. C, From D-ribitol-5 phosphate, treated with acid for 90 min. D, From D-ribitol-2 and ribitol-3 phosphate, treated with acid for 90 min. E, From ribitol 1 : 2-(hydrogen phosphate) from CDP-ribitol.

A mixture of YS and PS, separated from ribitol-1(5) phosphate on a long chromatogram, was treated with prostate phosphatase. The original compounds disappeared and ribitol was produced, together with a trace of anhydroribitol. The significance of the anhydroribitol will be discussed later. Treatment of YS and PS with acid gave the typical mixture



of compounds produced by acid treatment of ribitol-1(5) phosphate. A sample of yeast adenylic acid, which had been shown by ion-exchange chromatography to be a mixture of the 2′- and 3′-isomers, was hydrolysed by Dowex-50 resin (H^+ form). The mixed ribose phosphates were reduced with sodium borohydride to the ribitol phosphates and examined on paper. Two spots were obtained, identical in R_F values and colour reactions with YS and PS. The effects of prostate phosphatase and of acid on these ribitol phosphates were the same as those on YS and PS with the exception that phosphatase action yielded no anhydroribitol. When the ribitol-2 and -3 phosphate obtained from yeast adenylic acid were heated with N-hydrochloric acid and the 1(5)-phosphate, which was produced, subjected to the chemical degradation and enzymic test to establish its configuration, it was found to be completely racemised. These observations proved that YS and PS were ribitol-2(4) and -3 phosphate. It remained only to decide which of these structures corresponded to each spot.

Ribitol 1 : 2(4 : 5)-(hydrogen phosphate) was readily hydrolysed in sodium hydroxide solution to a mixture of two ribitol phosphates. One of these corresponded with the 1(5)-phosphate and the other must be ribitol-2(4) phosphate (IX), since phosphate migration does not occur in alkali. The latter corresponded with PS. Hydrolysis of CDP-ribitol with dilute aqueous sodium hydroxide also gave the 1(5)-phosphate and PS. YS was not formed and is therefore the 3-phosphate. Compounds analogous to YS and PS are produced when mannitol-1(6) phosphate is treated with acid.

The trace of anhydroribitol produced when YS and PS were treated with prostate phosphatase probably arose from traces of anhydroribitol phosphate(s) in these spots. No ribitol can be detected during acid hydrolysis of ribitol phosphates under our conditions. Since free ribitol itself would yield some anhydro-compound under these conditions it is probable that some anhydroribitol phosphate would be present.

The configuration of the ribitol phosphate residue in CDP-ribitol is of some biochemical importance. Although the function of CDP-ribitol is still unknown, it probably

participates as a coenzyme or intermediate in the metabolism of ribitol and its phosphate. It is reasonable to assume that the ribitol phosphate residue will be related metabolically to some naturally occurring pentose. As it is now shown that this residue is D-ribitol-5 phosphate (equivalent to L-ribitol-1 phosphate) (III), it follows that it and CDP-ribitol are related to either D-ribose-5 phosphate or D-ribulose-5 phosphate. Both these pentose phosphates occur as interconvertible intermediates in glucose metabolism in many living cells and it is not yet possible to determine which is more directly related to the nucleotide. It is interesting that, although the reversible reduction of aldoses and ketoses to polyols by bacteria is well known, only recently have similar reductions been observed with their phosphoric esters. A microbial enzyme has now been described which catalyses the reversible reduction of fructose-6 phosphate to D-mannitol-1 phosphate,[9] and a similar but less specific enzyme present in silkworm blood readily reduced D-ribose-5 phosphate to ribitol phosphate in the presence of triphosphopyridine nucleotide.[10]

Experimental

Oxidation of D-*Ribitol* 4 : 5-(*Hydrogen Phosphate*).—D-Ribitol-5 phosphate was cyclised by the use of trifluoroacetic anhydride as described earlier.[3] The cyclic phosphate (*ca.* 2 mg.) was purified by paper chromatography in solvent system (1). Pure D-ribitol 4 : 5-(hydrogen phosphate) was obtained by eluting the appropriate area of the paper and evaporating the eluate to dryness *in vacuo*. The residue was dissolved in sodium metaperiodate solution (80 μl., containing 150 mg./ml.) and the pH was kept at 5—6 by the addition of micro-drops of dilute sodium hydroxide solution. After 30 min. bromine (5—10 μl.) was added to the mixture with stirring, together with dilute sodium hydroxide solution to pH 7. After a further 1 hr. the pH had fallen to *ca.* 4 and solid inorganic material was removed by centrifugation. The yellow supernatant solution was evaporated to dryness *in vacuo* on a Polythene plaque. The residue was dissolved in water (0·1 ml.), and some solid inorganic material was removed by centrifugation. The supernatant solution was passed through a Dowex-50 (H^+ form) resin column (2 × 0·5 cm.). The column was washed with water, and the acid eluate (*ca.* 0·5 ml.) was collected. After 30 min. it was neutralised with ammonia and after suitable adjustment of the volume the products were resolved by paper chromatography run in solvent system (1) (descending front, 16 hr.). The area of the paper containing the D-glyceric acid phosphates was eluted. In some experiments a trace of a slower-running phosphate was observed. No inorganic phosphate was detected. The solution of pure D-glyceric acid phosphate thus obtained (sample A) was adjusted to a volume of *ca.* 120 μl. and samples were used in the following experiments.

Action of Prostate Phosphatase on the Product of Oxidation of D-*Ribitol* 4 : 5-(*Hydrogen Phosphate*).—Solution A (40 μl., containing *ca.* 300 μg. of D-glyceric acid phosphate) was mixed with 0·4M-ammonium acetate buffer (40 μl., pH 5·5) and a preparation [3] of prostate phosphatase (20 μl.). The mixture was kept under toluene at 37° for 36 hr. A sample of authentic D-glyceric acid phosphate was treated similarly. After suitable adjustment of the volume the products were subjected to paper chromatography in solvent systems (1), (2), and (3), and after drying were sprayed with reagents for phosphates and α-glycols.[11, 12] The oxidation product and D-glyceric acid phosphate were indistinguishable (R_P values are given in Table 2).

These experiments were repeated with samples of the oxidation products obtained from racemic ribitol cyclic phosphate (see below) and the cyclic phosphate derived from CDP-ribitol. Results were identical in all cases.

Production of Racemic Glyceric Acid Phosphate.—The barium salt of D-ribitol-5 phosphate (8 mg.) was heated with N-hydrochloric acid (0·5 ml.) for 30 min. at 100° in a sealed tube. The solution was evaporated to dryness; the residue was dissolved in water (40 μl.) and passed through a Dowex-50 (H^+ form) resin column (2 × 0·5 cm.) which was then washed with water. The acid eluate and washings were collected, neutralised with ammonia, evaporated to 80 μl.,

[9] Wolff and Kaplan, *J. Biol. Chem.*, 1956, **218**, 849.
[10] Faulkner, *Biochem. J.*, 1956, **64**, 436.
[11] Hanes and Isherwood, *Nature*, 1949, **164**, 1107.
[12] Buchanan, Dekker, and Long, *J.*, 1950, 3162; Baddiley, Buchanan, Handschumacher, and Prescott, *J.*, 1956, 2818.

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and applied to the baseline of a chromatogram paper. After chromatography (16 hr., descending front) in solvent system (1) the paper was dried and the area containing ribitol-1(5) phosphate was eluted. After evaporation (to 40 μl.) the solution was passed through a Dowex-50 (H^+ form) resin column (2 × 0·5 cm.) and the eluate (*ca.* 0·3 ml.) was collected and freeze-dried in a bulb-tube (*ca.* 3 ml. capacity). To the syrupy residue was added trifluoroacetic anhydride (1·0 ml.). The bulb-tube was sealed and shaken for 1 hr. Excess of trifluoroacetic anhydride was removed *in vacuo* and the syrupy residue was treated with ammonia (*d* 0·88, 120 μl. in water, 40 μl.). The product was run on paper as a band in solvent system (1) (ascending front). The subsequent elution and oxidation procedure were as described above, except that 120 μl. of sodium periodate solution were used. Sample B of glyceric acid phosphate was thus obtained.

The procedure was repeated on the barium salt of D-ribitol-5 phosphate (25 mg.) racemised for 1·5 hr. in N-hydrochloric acid at 100° (when about 50% breakdown to phosphoric acid and anhydroribitol occurs) (glyceric acid phosphate, sample C), and with a similarly racemised mixture from D-ribitol-2 and -3 phosphate from yeast adenylic acid (glyceric acid phosphate, sample D).

Glyceric Acid Phosphate from CDP-ribitol.—CDP-ribitol solution (140 μl. containing 2·8 mg. of nucleotide) was heated in a sealed tube with ammonia (*d* 0·88, 150 μl.) for 30 min. at 100°. After evaporation to dryness the residue was dissolved in water (80 μl.) and run on paper as a band in solvent system (1) (ascending front). The cyclic phosphate was eluted from the appropriate area of the paper and was subjected to oxidative degradation to glyceric acid phosphate in the manner already described (sample E).

Determination of Phosphate in Samples A—E.—The phosphate content (in terms of glyceric acid phosphate) of each of the samples was determined in duplicate by Allen's method.[13] Control determinations were carried out on solutions which had passed through all the stages described. The average control value in all the runs was +0·024 μmole of phosphate per 10 μl. of sample. This is allowed for in values reported in Table 1.

Enzymic Assay of D-*Glyceric Acid Phosphate in Samples* A—E.—*Materials.* Enzyme: a freeze-dried sample of rabbit muscle enzyme was prepared by Racker's method,[14] the fraction being used which was precipitated between 50% and 72% ammonium sulphate saturation.[15] Reduced DPN: a sample supplied by C. F. Boehringer & Sons, Mannheim, and containing 64% of DPNH was used. Phosphate buffer: 0·01M-potassium dihydrogen phosphate solution was treated dropwise with concentrated potassium hydroxide solution until the pH had risen to 7·3. Magnesium sulphate: an aqueous solution containing 100 μmoles/ml. ATP: a 0·05M-solution of the Na/K salt. The rabbit muscle contains myokinase and other enzymes which convert ATP into the diphosphate required for the production of lactate from glyceric acid phosphate.

Method. In a 1 cm. silica cell were placed phosphate buffer (3·0 ml.), DPNH (*ca.* 1·4 mg.) to give an optical density of *ca.* 2·5 at 340 mμ, magnesium sulphate solution (0·05 ml.), ATP solution (0·05 ml.), and freeze-dried rabbit muscle enzyme (100—200 μg.). Variation in the amount of enzyme added merely altered the rate at which D-glyceric acid phosphate was consumed and had no effect on the amount of DPNH oxidised. The optical density of the solution at 340 mμ was recorded at convenient intervals. After a slight initial fall in optical density a steady reading was observed. The glyceric acid phosphate (10 μl.) was added and the fall in optical density at 340 mμ was recorded until the reading was again constant (10—30 min.). It was found in separate experiments that glyceric acid phosphate was not consumed unless both magnesium and ATP were present.

Samples A—E were examined in duplicate and the amount of D-phosphate present in 10 μl. was calculated on the assumption that one equiv. of it consumed one equiv. of DPNH, a value of ε 6220 at 340 mμ being used for DPNH. The results are shown in Table 1.

Action of Phosphatase on "PS" and "YS."—The barium salt of D-ribitol-5 phosphate (2 mg.) was heated with N-hydrochloric acid in a sealed tube for 15 min. at 100°. After removal of barium with a little Dowex-50 (H^+ form) resin and evaporation to dryness *in vacuo*, the hydrolysis products were resolved by paper chromatography as a band in solvent system (1) using a descending front (20 hr.). PS and YS were eluted from the appropriate area of the

[13] Allen, *Biochem. J.*, 1940, **34**, 858.
[14] Racker, *J. Biol. Chem.*, 1947, **167**, 843.
[15] Ratner and Pappas, *ibid.*, 1949, **179**, 1197.

paper on to a small Polythene plaque, with subsequent evaporation of solvent *in vacuo* (P_2O_5). In this way, although it was not possible to achieve a complete separation of PS and YS from each other, they were obtained free from the other products of acid action (ribitol-1(5) phosphate, anhydroribitol, and phosphoric acid).

A part of the mixture was incubated at 37° for 16 hr. with prostate phosphatase in 0·2M-ammonium acetate buffer (pH 5·5). A second part was heated with N-hydrochloric acid at 100° for 15 min. and solvent was removed *in vacuo*. The products of these reactions were examined, together with a sample of unchanged material in solvent system (1). Products were detected by spraying the dried paper with the molybdate reagent for phosphoric esters and the periodate–Schiff reagents for glycols. Phosphatase action completely destroyed PS and YS, yielding ribitol, inorganic phosphate, and a trace of anhydroribitol, indistinguishable in behaviour from the authentic materials. Short acid treatment of PS and YS produced the typical acid hydrolysis mixture observed with all ribitol phosphates.[3]

Synthesis of a Mixture of D-*Ribitol-2 and -3 Phosphate.*—Yeast adenylic acid (150 mg.) was added rapidly, with stirring, to Dowex-50 (H^+ form) resin (1·5 ml.) in water (1·5 ml.) at 100°. After 5 min. at this temperature the mixture was cooled in an ice-bath and the resin was filtered off and washed with water (2 ml.). The filtrate contained much organic phosphate, a little inorganic phosphate, and no ultraviolet-absorbing material. After adjustment to pH 8 with dilute ammonia, sodium borohydride (22 mg.) was added with stirring. The course of the reduction was followed at intervals by examining samples on filter paper with the aniline phthalate spray reagent.[16] Reduction was almost complete after 1 hr. but a further 2 hr. was allowed to complete the reaction. Acetic acid (0·15 ml.) was added to decompose the excess of borohydride, followed by water (to 60 ml.) and ammonia to pH 8. The solution which was N/24 with respect to ammonium acetate was passed through a column of Amberlite IRA-400 (acetate form) resin (6 × 1 cm.), and borate was eluted with M/24-ammonium acetate solution (50 ml.). The phosphates were eluted with M-ammonium acetate solution (20 ml.). The eluate was stirred with Dowex-50 (H^+ form) resin (12 ml.), then filtered, and the resin was washed with a little water. Filtrate and washings were evaporated to small volume *in vacuo* below 40°. Residual acetic acid was removed by distillation *in vacuo* below 40°. The remaining oil was distilled with 5 portions (each of 20 ml.) of anhydrous methanol to remove traces of boric acid. The residue was dissolved in water (5 ml.) and 0·1N-barium hydroxide was added to pH 9. Excess of barium was precipitated by the addition of a little solid carbon dioxide. After evaporation *in vacuo* to 5 ml., barium phosphate and carbonate were removed by centrifugation. Alcohol (5 ml.) was added to the supernatant liquor, and the precipitated barium salt was centrifuged off, washed with acetone, and dried. It was purified by redissolving it in water (5 ml.), centrifuging off a small insoluble residue, and treating the supernatant liquid with acetone (10 ml.). The precipitated salt was washed with acetone and dried *in vacuo* (Found: P, 8·2. Calc. for $C_5H_{11}O_8PBa$: P, 8·4%).

According to Khym, Doherty, and Cohn [17] the salt should consist of *ca.* 60% of ribitol-3 phosphate and 40% of D-ribitol-2 phosphate. These authors hydrolysed yeast adenylic acid by a method similar to that described above and reduced the ribose phosphates by catalytic hydrogenation.

Experiments with the Mixture of Ribitol-2 and -3 Phosphate.—Barium ions were removed from a small sample of the salt by treatment with a little Dowex-50 (H^+ form) resin. The sample was examined by chromatography in solvent system (1), a descending front being used and the solvent allowed to drip (20 hr.). A typical acid-treated sample of ribitol-1(5) phosphate was examined concurrently. Papers were sprayed with reagents for the detection of phosphates and α-glycols. Ribitol-2(4) and -3 phosphate were incompletely separated and were indistinguishable from PS and YS. The synthetic mixture contained no detectable ribitol-1(5) phosphate or inorganic phosphate. Short acid treatment of the mixture gave results identical with those already described for a similar treatment of a mixture of PS and YS. Enzymic dephosphorylation of the synthetic mixture yielded ribitol and inorganic phosphate. (No trace of anhydroribitol was detected.)

Alkaline Hydrolysis of CDP-ribitol.—CDP-ribitol (400 μg.) in water (20 μl.) was heated with 2N-sodium hydroxide (20 μl.) in a sealed tube at 100° for 30 min. Sodium ions were removed with a little Dowex-50 (H^+ form) resin, ammonia was added to neutrality and, after suitable

[16] Partridge, *Nature*, 1949, **164**, 443.
[17] Khym, Doherty, and Cohn, *J. Amer. Chem. Soc.*, 1954, **76**, 5525.

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adjustment of the volume, the mixture was examined by paper chromatography with descending front in solvent system (1) (20 hr.). The products were cytidine-5′ phosphate, ribitol-1(5) phosphate, and PS. The ribitol phosphates were present in comparable amounts, with the 1(5)-phosphate slightly predominating. No YS or inorganic phosphate was detected.

Alkaline Hydrolysis of Ribitol 1 : 2-*(Hydrogen Phosphate)*.—This was carried out in a manner similar to that described for CDP-ribitol. The ribitol phosphates formed were indistinguishable from those obtained from the nucleotide.

The Behaviour of Ribitol Phosphates with the Periodate–Schiff Reagents.—Ribitol-1(5) and -2(4) phosphate behave similarly towards the periodate–Schiff spray reagents, *i.e.*, a purple-red colour is rapidly formed which later intensifies and deepens to purple. This behaviour is typical of acyclic polyols. Only a little of the 2(4)-isomer is produced by acid treatment of ribitol-1(5) phosphate—sufficient to give a weak phosphate reaction and a weak purple colour with the glycol reagents after several hours, but insufficient to produce the initial purple-red colour. Ribitol-3 phosphate also gives the initial purple-red colour, but after a few minutes a strong yellow colour is superimposed on the purple-red area and is seen as a yellow halo. The amount of ribitol-3 phosphate formed during acid treatment of ribitol-1(5) phosphate is too small for detection by the phosphate spray reagents applied to paper chromatograms containing normal amounts (*ca.* 100 μg.) of total phosphates. However, the yellow colour reaction with the periodate–Schiff reagents is clearly shown on such papers.

Inositol phosphate gives a yellow colour with the latter reagents.

Paper Chromatography.—Whatman No. 4 paper was washed with 2N-acetic acid, then water. The following solvent systems were used :

(1) *n*-Propyl alcohol–ammonia (*d* 0·88)–water (6 : 3 : 1); (2) *n*-butyl alcohol–acetic acid–water (organic layer) (4 : 1 : 5); (3) *n*-butyl alcohol–ethanol–water (organic layer) (4 : 1 : 5). Ascending front chromatography was employed.

TABLE 2.

	R_F in solvents :		
	(1)	(2)	(3)
CDP-ribitol	0·33	—	—
Ribitol-1 phosphate	0·34	—	—
Ribitol-2 phosphate (PS)	0·39	—	—
Ribitol-3 phosphate (YS)	0·39	—	—
Ribitol 1 : 2-(hydrogen phosphate)	0·53	—	—
Anhydroribitol	0·87	—	—
Glyceric acid phosphate	0·20	0·23	0·07
Glyceric acid	0·53	0·34	0·12
Ribitol	0·76	0·34	0·34

The following distances of migration were observed in solvent system (1), when a descending front was used and the solvent allowed to drip : ribitol-1 phosphate, 21·6 cm.; ribitol-2 phosphate, 25·1 cm.; ribitol-3 phosphate, 26·1 cm.

We are grateful to Dr. G. R. Greenberg for helpful advice on the enzyme experiments. We thank the Nuffield Foundation and the Rockefeller Foundation for grants and the Council of King's College for the award of a George Angus Studentship (to B. C.).

KING'S COLLEGE, UNIVERSITY OF DURHAM,
NEWCASTLE UPON TYNE.

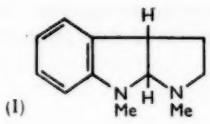
[*Received, November 15th*, 1956.]

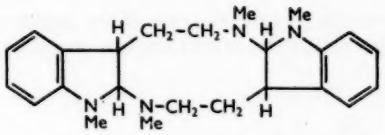
354. *The Structure of Folicanthine. Part II.*[1]

By H. F. Hodson and G. F. Smith.

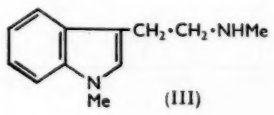
The alkaloid folicanthine is shown to have structure (II).

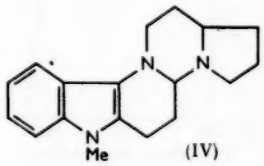
The alkaloid folicanthine, first isolated from the leaves of *Calycanthus floridus* L. by Eiter and Svierak[2,3] in 0·34% yield, has now been isolated from the leaves of *C. occidentalis* Hook and Arn. in 0·14% yield. Earlier[1] we identified the main degradation products obtained by Eiter and Svierak[3] and discussed two possible structures, (I and II), for the

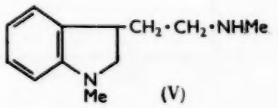

(I)


(II)

alkaloid. These structures are based mainly on the conversion of the alkaloid in 8N-hydrochloric acid[3] into 1-methyl-3-2′-methylaminoethylindole (III), the yield of which, being of the order of 50%, leaves open the possibility of the undetected loss of a non-indolic nitrogen-containing fragment, as indeed was postulated by Eiter[3] when he proposed structure (IV) for folicanthine.


(III)


(IV)


(V)

We now find that an excellent yield (86% as the pure dipicrate) of the indoline (V) is obtained from folicanthine by use of zinc and 5N-hydrochloric acid. This high yield rules out a structure such as (IV) containing three nitrogen atoms and clearly indicates that the structure must be made up of one or more dimethyltryptamine (III) units only.

Oxidation of folicanthine by silver acetate to 9-methylnorharman (XII)[1,3] suggests the presence of a hexahydro-β-carboline system: the ease of conversion of folicanthine into the indoles (III) and (V) cannot, however, be accounted for in terms of such a system, but follows naturally from a *gem*-diaminoeserine-like system. This is supported (Figs. 1—3) by the ultraviolet spectra. Folicanthine has an indoline-type spectrum, which is retained in acid solution though with hypsochromic shift of about 10 mμ for both bands (Fig. 1). Eserine and calycanthine behave in the same manner. In acid solution the absorbing species is a cation (VI), in which the formal positive charge on N(*b*) has rendered N(*a*) virtually non-basic: the N(*a*)-electron-pair is thus still able to resonate with the benzene ring, with retention of indoline-type absorption. The hypsochromic shift must be a result of the closeness of the positive charge on N(*b*) to the mesomeric system.

Deoxydihydroajmaline (VII) has a hexahydro-β-carboline type of structure; its ultraviolet absorption spectrum is also that of an indoline, but in this case acidification does not appreciably change the spectrum (Fig. 2). Here again we have a monoacidic base, N(*a*) having become practically non-basic as a result of the positive charge on N(*b*) in the cation: as a result, the indoline-type absorption is retained in acid solution. The

[1] The communication by Hodson and Smith, *Chem. and Ind.*, 1956, 740, is considered to be Part I.
[2] Eiter and Svierak, *Monatsh.*, 1951, **82**, 186.
[3] *Idem, ibid.*, 1952, **83**, 1453.

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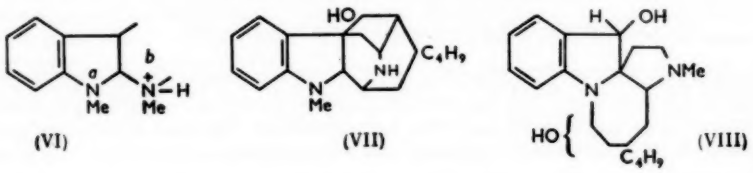
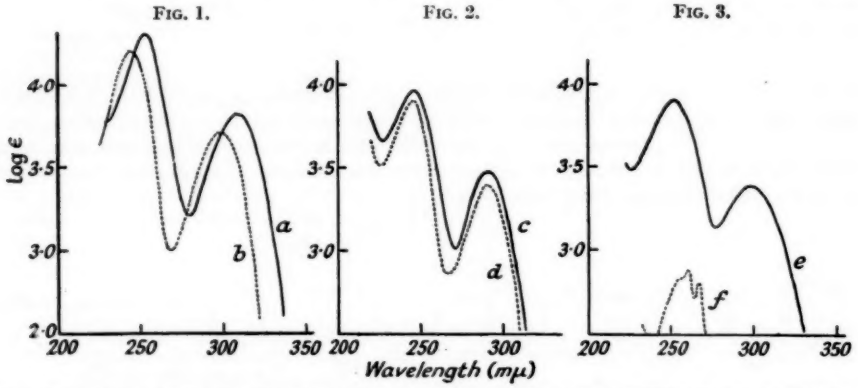
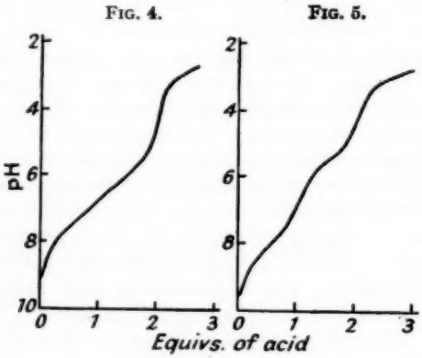
positive charge on N(*b*), however, is now no longer sufficiently close to the mesomeric system, and there is no appreciable shift of the bands. ε_1-Hexahydrofluorocurine (VIII), a hexahydro-β-carboline analogue, is reported to behave in the same manner.[4]



To complete the picture, the case of the indoline (V) may be mentioned. Its indoline-type absorption disappears in acid and is replaced by the benzenoid absorption of anilinium-



Absorption spectra of (Fig. 1) *folicanthine* (II) (*a*) *in* EtOH *and* (*b*) *in* HCl–EtOH, (Fig. 2) *deoxydihydro-ajmaline* (VII) (*c*) *in* EtOH *and* (*d*) *in* HCl–EtOH, *and* (Fig. 3) **1-*methyl*-3-2′-*methylaminoethylindoline** (V) (*e*) *in* EtOH *and* (*f*) *in* HCl–EtOH.



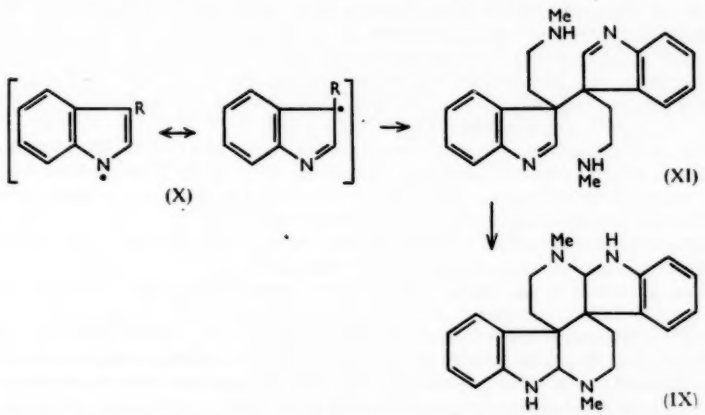
Potentiometric titration curve of (Fig. 4) *folicanthine and* (Fig. 5) *calycanthine in* 60% *aqueous ethanol.*

type ions (Fig. 3). In (V) the positive charge on the protonated N(*b*) is sufficiently far away from N(*a*) not to prevent it from being protonated in dilute aqueous acid. In contrast with (VI), (VII), (VIII), the base (V) is thus diacidic in dilute aqueous acid, and it forms a dipicrate.

[4] Bickel, Schmid, and Karrer, *Helv. Chim. Acta*, 1955, **38**, 654.

We are thus left with the alternatives (I) and (II) for folicanthine. Eiter and Svierak [3] reported a molecular weight of 297 by Rast's method in bornylamine: this falls between 188 for (I) and 376 for (II). In triplicate determinations by Rast's method in camphor, we obtained values of 384, 376, and 379; in addition, one determination by Barger's isothermal distillation method in benzene gave a value of 375. These results lead us to propose structure (II) for folicanthine.

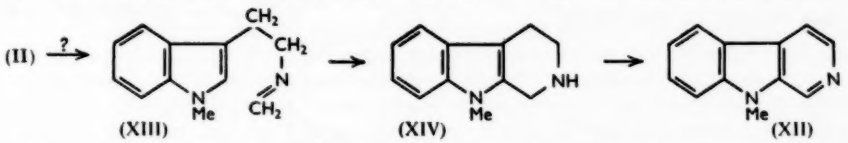
Attempts to prove structure (II) chemically by preparing a monosalt or a mono-substitution product have failed. The titration curve of folicanthine (Fig. 4), however, provides convincing evidence in favour of structure (II). The curve is not that expected of a monoacidic base, but falls into the category of diacidic bases and dibasic acids with a ΔpK_a of the order of 1·2. This conclusion is based on Auerbach and Smolczyk's work,[5] who made a thorough theoretical and experimental study of the change in shape of the titration curve of dibasic acids with change of ΔpK_a. For folicanthine the ΔpK_a is of the order of 1·4 (all titrations were carried out in 60% ethanol). The much stronger base putrescine has ΔpK_a 1·3, and its titration curve is almost identical with that of folicanthine.



Calycanthine (IX), with the larger ΔpK_a (about 2·2), has a titration curve with two inflexions (Fig. 5).

That the ΔpK_a of calycanthine is greater than that of folicanthine is probably due to the fact that structure (IX) requires the two basic centres to be closer together than in structure (II).

Folicanthine is thus seen to be very closely related structurally to calycanthine [6] (IX). The main difference is the absence in folicanthine of a bond uniting the β-positions of the two indole nuclei; the other difference is that the N(*a*) atoms of folicanthine are methylated. If we accept the view [7] that the biogenesis of calycanthine involves a free-radical dimerisation of two tryptamine units as portrayed in (X) ⟶ (XI), we can see a possible reason



for the non-existence of a ββ-link in folicanthine in the inability of a precursor carrying a methyl group on the indole nitrogen [say (III)] to form a free radical of type (X).

[5] Auerbach and Smolczyk, *Z. phys. Chem.*, 1924, **110**, 65.
[6] Robinson and Teuber, *Chem. and Ind.*, 1954, 783.
[7] Harley-Mason, personal communication.

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The formation of 9-methylnorharman (XII) by oxidation of folicanthine with silver acetate in boiling 1% aqueous acetic acid remains to be accounted for. The tryptamine (III) is completely resistant to this reagent, so that preliminary breakdown of folicanthine to (III) must be ruled out. Whatever mechanism operates, it is evident that the *N*(*b*)-methyl group becomes the $C_{(1)}$ of the harman system, probably by way of (XIII) and (XIV).

Experimental

M. p.s are corrected.

Extraction of Calycanthus occidentalis *Leaves.*—The dry, powdered leaves (740 g.) were extracted continuously with light petroleum (b. p. 60—80°) for 36 hr., the petroleum then distilled off, and the residue dissolved in ether (3 l.). The solution was extracted three times with 5% aqueous tartaric acid (120, 60, 60 c.c.), and the combined acid extracts were washed with ether, basified with aqueous sodium hydroxide, and repeatedly extracted with ether. The dried (K_2CO_3) ether extracts yielded practically pure folicanthine, m. p. 116—119° (677 mg.). After passage through a short alumina column in ether to remove traces of colour, the base was twice crystallised from ether–light petroleum (b. p. 30—40°), then forming colourless prisms, m. p. 118—120°. The extraction of the leaves was continued for 48 hr. after basification with triethylamine (20 c.c.). The extract was worked up as above and yielded a further quantity of fairly pure folicanthine (403 mg.). The total yield of alkaloid was 1·08 g., 0·144%. Light absorption : $\lambda_{max.}$ 2540 (log ε 4·249), 3110 Å (log ε 3·826).

Reduction of Folicanthine.—A solution of folicanthine (96 mg.) in 5N-hydrochloric acid (15 c.c.) was treated on the steam-bath with granulated zinc (5 g.) at a rate sufficient to maintain a vigorous evolution of hydrogen. After 1½ hr. the cooled solution was filtered, diluted to 30 c.c., basified with aqueous ammonia, and extracted with ether (4 × 20 c.c.); the combined dried extracts yielded a colourless viscous oil (94·4 mg.). This oil, with picric acid (250 mg.) in methanol (5 c.c.), gave the *dipicrate*, m. p. 161—165° (272 mg.). Concentration of the mother-liquor yielded a further 6 mg. (total, 86%). One crystallisation from acetone gave yellow prisms, m. p. 162—165°, unchanged by further crystallisation and undepressed by synthetic 1-methyl-3-2′-methylaminoethylindoline picrate (Found : C, 44·9; H, 4·2; N, 17·5. $C_{12}H_{18}N_2.2C_6H_3O_7N_3$ requires C, 44·5; H, 3·7; N, 17·3%). The free base, recovered from the picrate and distilled at 80—100° (oil bath)/5 × 10^{-5} mm., had ultraviolet (in absolute ethanol) and infrared (liquid film) spectra identical with those of synthetic 1-methyl-3-2′-methylaminoethylindoline.

1-*Methyl*-3-2′-*methylaminoethylindoline* (V).—1-Methyl-3-2′-methylaminoethylindole (23·0 mg.) was reduced by zinc and acid as described above. The product was a colourless oil (22·5 mg.), converted by picric acid (56 mg.) in methanol (1 c.c.) into 1-methyl-3-2′-methylaminoethylindoline dipicrate (57·5 mg., and second crop of 5 mg.) which crystallised from acetone as yellow prisms, m. p. 164—166° unchanged on further crystallisation (Found : C, 44·8; H, 4·1%). Light absorption of the free base in ethanol : $\lambda_{max.}$ 2540 (log ε 3·902), 3000 Å (log ε 3·388).

The authors are indebted to the Curator of the Royal Botanic Gardens, Kew, Mr. W. M. Campbell, for supplying leaves of *Calycanthus occidentalis*. The work was carried out during the tenure of a grant from the Schunck Fund of the University of Manchester (H. F. H.).

The University, Manchester. [*Received, December 13th,* 1956.]

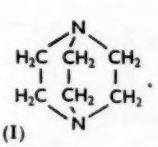
355. *Triethylenediamine (1 : 4-Diazabicyclo[2 : 2 : 2]octane) and Hexaethylenetetramine. Part III.* The Interaction of 2 : 2′ : 2″-Trichlorotriethylamine Hydrochloride and Dimethylamine.*

By Frederick G. Mann and F. C. Baker.

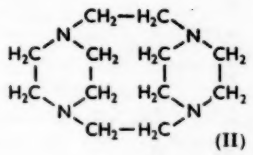
Interaction of 2 : 2′ : 2″-trichlorotriethylamine monohydrochloride and methanolic dimethylamine, and thermal decomposition of certain of the products, have been re-investigated in detail. No evidence for the formation of hexaethylenetetramine during these decompositions has been obtained, the main high-boiling product being 1 : 2-di-(4-methyl-1-piperazinyl)ethane.

Four disubstituted piperazines which occur in this work are of almost identical composition. To aid the necessary accurate identification, a series of highly purified derivatives of each base has been prepared, and the m. p. of each derivative determined under specified conditions.

Mann and Mukherjee investigated the interaction of 2 : 2′ : 2″-trichlorotriethylamine monohydrochloride, $(Cl{\cdot}CH_2{\cdot}CH_2)_3N,HCl$, with methanolic dimethylamine and stated that thermal dissociation of one of the products of this reaction gave rise to triethylenediamine (I) and hexaethylenetetramine (II). In view of the criticisms of certain aspects of this work by Hromatka and Kraupp,[2] we have carried out



(I)



(II)

a thorough investigation of the above subject, and, by working on a considerably larger scale, have been able in particular to separate the products of the thermal decomposition by fractional distillation, in place of the unsatisfactory fractional crystallisation of their picrates previously employed. We have thus been able to extend considerably the range of this investigation, and to correct certain of the earlier statements.[1]

We find that a mixture of trichlorotriethylamine hydrochloride and a 40% (w/v) solution of methanolic dimethylamine (3·4 mols.), when set aside at room temperature for 24 hours or heated at 45—50° for 1·5 hours, and then worked up with hydrogen chloride, gives the monohydrated 1-2′-chloroethyl-4 : 4-dimethylpiperazinium chloride hydrochloride (III) : this product is also obtained when the proportion of dimethylamine is varied from 2·0 to 6·6 mols. with the above heating. The salt (III), hydrated or anhydrous, has m. p. 264° with two well-defined stages of effervescence (p. 1886). A methanolic solution of the salt (III), when shaken with silver oxide, filtered, and treated with methyl iodide (*a*) in the cold, or (*b*) boiling under reflux, gives the piperazinium iodide (IV) or the iodide methiodide (V) respectively.

When trichlorotriethylamine hydrochloride is heated with the methanolic dimethylamine (12·8 mols.) at 40—45° for 8 hours, the product after similar working up is 1-2′-dimethylaminoethyl-4 : 4-dimethylpiperazinium chloride dihydrochloride (VI), m. p. 227—228°. The hydrochloride, when heated however with the methanolic dimethylamine (10·7 mols.) at 125° for 7 hours, yields 1-2′-dimethylaminoethyl-4-methylpiperazine trihydrochloride (VII), m. p. 262° after crystallisation, 270° after sublimation. The identity of the salt (VII) is shown by the fact that concentrated aqueous alkalis liberate

* Part II, Mann and Senior, *J.*, 1954, 4476.

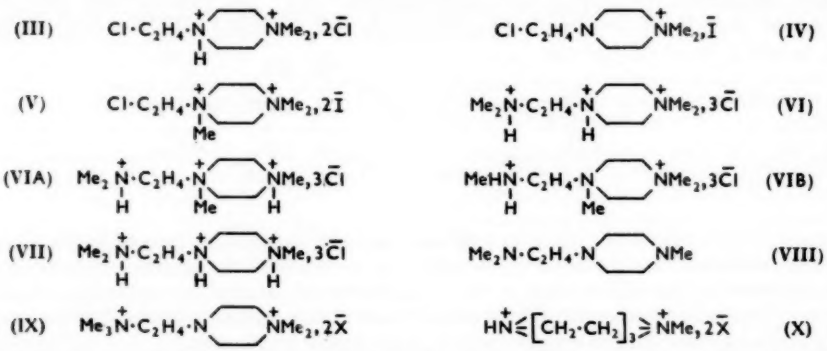
[1] Mann and Mukherjee, *J.*, 1949, 2298.

[2] Hromatka and Kraupp, *Monatsh.*, 1951, **82**, 880.

the base (VIII), b. p. 94°/12 mm. : hence the salt cannot contain a quaternary ammonium chloride group which any other formulation would entail.

Hromatka and Kraupp [2] state however that the hydrochloride, when heated with 55·7% (w/w) methanolic dimethylamine (3·57 mols.) at 45° for 100 min., gives a mixture of the salt (III), m. p. 260—262°, and the salt (VI), m. p. 305—307°, and when heated with 40% methanolic dimethylamine (13·1 mols.*) at 125° for an unspecified time gives the salt (VII), m. p. 265—266°.

Our results above were obtained independently of (and before the publication of) the results of Hromatka and Kraupp. They agree well, except for the marked difference in the m. p. of the salt (VI), which would indicate that the salts described are structurally different. The following points are therefore noteworthy. (*a*) We have carried out the preparation of our salt, m. p. 228°, on numerous occasions, and have repeatedly checked its m. p. and composition. (*b*) Our salt crystallises from 97% ethanol as a monohydrate, which when confined over phosphoric anhydride at 20 mm. gives the anhydrous salt, having an identical m. p. Hromatka and Kraupp's salt, when crystallised from ethanol formed a dihydrate, which was unaffected by confinement over phosphoric anhydride in a high vacuum : when heated at 140° in this vacuum it decomposed. (*c*) The structure of the chloroethyl salt (III) is not in reasonable doubt. Since the salt (VI) arises when the



conditions of preparation of (III) are changed only by increasing the proportion of dimethylamine and the time (but not the degree) of heating, a comparatively simple reaction, such as the conversion of the initial chloroethyl group of (III) into the dimethylaminoethyl group, would be expected. It is very difficult to visualise the formation in these circumstances of any isomeric salt such as (VIA) or (VIB). The formation of the salt (VIA) would involve degradation of the terminal (N^4) quaternary chloride to the tertiary hydrochloride, and quaternisation of the tertiary (N^1) group : that of the salt (VIB) would involve conversion of the initial 2′-Me_2N-group into a MeNH-group, with quaternisation of the N^1 group as before. Although Hromatka and Kraupp [2] have shown that appropriate amines can be demethylated by an excess of dimethylamine, which is converted into trimethylamine, this process, like the degradation of a quaternary salt, requires a much higher temperature than that employed in the preparation of the salt (VI). (*d*) Our salt (VI), when heated just above its m. p., undergoes effervescence with the formation of the salt (VII). (*e*) The base (VIII), when treated with an excess of methanolic methyl bromide (with or without heating), gives a dimethobromide (IX; X = Br), and similarly with methyl iodide yields a dimethiodide (IX; X = I). A methanolic solution of the salt (VI), when shaken with silver oxide, filtered, and treated with these methyl halides under these conditions gives the same products. There is very little doubt that these dimethohalides have the structure (IX), for the inductive effect of the positive poles on

* Calculated on w/v basis : the basis is not specified by these authors.

the two outer quaternary nitrogen atoms would considerably deactivate the central tertiary nitrogen atom : this cumulative effect would not occur if the poles were on any other two of the nitrogen atoms. This is strong evidence for the structure of the salt (VI), and would be decisive if the quaternary ammonium group in the salt (III) undergoes no change during the conversion (III) ⟶ (VI).

We consider therefore that our salt, m. p. 228°, has almost certainly the structure (VI), but we cannot explain the different result obtained by Hromatka and Kraupp.[2]

The thermal decomposition of the salts (III), (VI), and (VII) has been studied in detail.

The salt (III), when heated at 250—254°, *i.e.*, until the first effervescence was complete, gave triethylenediamine hydrochloride methochloride (X; X = Cl), which was identified by treatment in methanolic solution with silver oxide and methyl iodide in turn, whereby triethylenediamine dimethiodide was obtained. Hromatka and Kraupp [2] decomposed the salt (III) at 270°, and isolated only piperazine and 1 : 4-dimethylpiperazine, both as derivatives.

Thermal decomposition of the salts (VI) and (VII) gave a mixture of amines. We have consequently submitted each salt, on a 250—300 g. scale, to decomposition at 280° at atmospheric pressure (*i.e.*, under the conditions employed by Mann and Mukherjee [1]), the crude product being then strongly basified and the liberated amines extracted with ether and then fractionally distilled. The properties of picrates of the amines thus isolated showed clearly that separation of the main components of the crude product by fractional crystallisation of their picrates, as described by Mann and Mukherjee,[1] without any preliminary fractional distillation, was unsatisfactory. On the other hand, the curiously volatile properties of triethylenediamine (I), had it occurred in these mixed amines, would have made its isolation from the mixture by distillation extremely difficult.

The properties of triethylenediamine must therefore be first discussed. We have prepared this base by a modification of Hromatka and Kraupp's method,[2] whereby triethylenediamine dimethobromide (prepared by the combination of 1 : 4-dimethylpiperazine and ethylene dibromide [1]) was heated at 230—240°/0·001 mm. in a glass vessel connected to a receiver cooled in carbon dioxide–acetone (p. 1890). The crystalline base slowly sublimed into the receiver, and when resublimed was obtained in large, exceedingly beautiful pure crystals, which were identified by analysis and by molecular-weight determinations in boiling ethanol and benzene. The base has m. p. 156—157° in a sealed tube : Hromatka [3] gives m. p. 158—160° in an evacuated tube, but we find that its ready sublimation in an evacuated tube (which occurs slowly even at room temperature) makes this determination unsatisfactory. The base readily sublimes when heated at 45°/15 mm., crystals forming on the cooler upper portions of the tube : this ready volatilisation is similar to that of the analogous quinuclidine recorded by Meisenheimer.[4] Furthermore, at room temperature the powdered amine steadily volatilises in a desiccator at 1 atm. containing paraffin wax shavings, and in a desiccator containing sodium hydroxide pellets at 15 mm. The amine is volatile in the vapour of boiling ethanol and benzene, but not appreciably so in that of ether. The difficulties attending the separation of the base from other amines by distillation are obvious.

The identity of the triethylenediamine (I) is further confirmed by its ready union with methyl bromide to re-form the original dimethobromide. Mann and Mukherjee,[1] who had available only salts of this base, sought evidence that the base was in fact the diamine and not hexaethylenetetramine, by determining the " apparent " molecular weight of this methobromide cryoscopically in dilute aqueous solution, where almost complete ionisation would have occurred. Hromatka and Kraupp [2] were subsequently unable to obtain similar results, but an independent series of determinations (p. 1891), kindly undertaken by Dr. A. Senior, confirms our earlier results. A number of derivatives of this diamine are recorded (see Table, p. 1885).

[3] Hromatka, *Ber.*, 1942, **75**, 1302.
[4] Meisenheimer, *Annalen*, 1920, **420**, 194.

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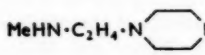
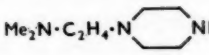
The thermal decomposition of the salts (VI) and (VII) at atmospheric pressure gave closely similar products: this was expected in view of the ready thermal conversion (VI) ⟶ (VII). In a typical experiment using the salt (VII), distillation of the ethereal extracts of the liberated amines gave the following fractions.

(A) The ether distillate. This contained much 1 : 4-dimethylpiperazine, which is readily volatile in boiling ether [5] and was isolated as its dihydrochloride.

(B) A fraction, b. p. 130—133°, of 1 : 4-dimethylpiperazine, from which a very small quantity of piperazine was also isolated.

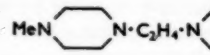
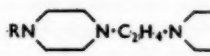
(C) A considerable fraction, b. p. 86—87°/12 mm., consisting of the base (VIII), contaminated with a base, $C_8H_{19}N_3$, which may have been the amine (XI) or the isomer (XII).

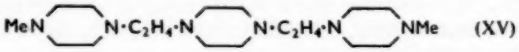
(D) A small fraction, b. p. 74—76°/0·01 mm., which initially appeared to consist mainly of hexaethylenetetramine (II), $C_{12}H_{24}N_4$. This base was purified by recrystallisation of its tetrahydrobromide, and when regenerated had b. p. 91°/0·03 mm., m. p. 40—43°. A number of derivatives of this base were prepared, particularly for comparison with those of triethylenediamine. Its behaviour on quaternisation, whereby a trimethobromide and -iodide were obtained, cast doubt on this identification, for the various conformations of hexaethylenetetramine, in which the two piperazine rings have the chair and/or the boat form, would usually allow only diquaternisation. The synthesis of 1 : 2-di-

(XI)   (XII)

(4-methyl-1-piperazinyl)ethane (XIII), $C_{12}H_{26}N_4$, was therefore kindly undertaken by Mr. H. R. Watson, who has obtained this amine by the hydrolysis of the diethoxycarbonyl derivative (XIV; R = CO_2Et), followed by formaldehyde–formic acid methylation of the hydrolysis product (XIV; R = H). Comparison of the two bases and certain of their crystalline derivatives showed undoubtedly that our amine obtained by thermal decomposition is the amine (XIII).

(E) On one occasion, a higher fraction, b. p. 105—108°/0·065 mm., was isolated: it was almost insoluble in water, whereas the amine (XIII) is freely soluble. Its molecular weight and the analyses of the base and its available derivatives indicated a molecular formula $C_{18}H_{36-38}N_6$. By analogy, it is highly probable that this amine is 1 : 4-di-[2-(4-methyl-1-piperazinyl)ethyl]piperazine (XV), $C_{18}H_{38}N_6$. It is unfortunate that the very small quantity of the amine available allowed only one molecular-weight determination, for the analysis of its salts would not differentiate between the amine (XV) and hexaethylenetetramine (II).

(XIII)   (XIV)

 (XV)

The products of the thermal decomposition of the salt (VI) differed from those of the salt (VII) only in that (*a*) fraction (B) now contained only a trace of piperazine, (*b*) fraction (C) was the almost pure amine (VIII), the partially demethylated amine $C_8H_{19}N_3$ being present in very small proportion, and (*c*) the fraction (E) was not detected.

Our investigation has therefore given no evidence for the formation of hexaethylenetetramine during the thermal decomposition of the salt (III), (VI), or (VII).

It is noteworthy that the triamine (VIII) gives a stable tri-hydrochloride, -hydrobromide, -picrate, and (hydrogen oxalate), but only the dihydriodide is sufficiently stable to allow crystallisation from hot solvents: the amine also forms only diquaternary salts

[5] Mann and Senior, *J.*, 1954, 4476.

(p. 1888). Similarly the tetramine (XIII) gives a stable tetra-hydrochloride, -hydrobromide, -picrate, and -(hydrogen oxalate), but only a trihydriodide and di- and triquaternary salts. It is clear in each case that progressive salt formation tends to deactivate the final tertiary nitrogen atom: this is insufficient to prevent formation of stable full salts by strong acids or by weak non-volatile acids but does prevent such formation by hydriodic acid. Salt formation by quaternisation apparently exerts this deactivating effect more powerfully than that by proton addition.

There has clearly in the past been considerable confusion in this section of piperazine chemistry, which we have been at pains to clarify in the derivatives discussed above. Particular difficulty can arise here, because: (*a*) both 1 : 4-dimethylpiperazine and the base (VIII) have the empirical formula $(C_3H_7N)_n$ ($n = 2$ or 3), and the diamine (I) and the tetramine (XIII) have the formulæ $C_6H_{12}N_2$ and $C_{12}H_{26}N_4$ respectively, so that analysis of these amines or their normal derivatives is virtually useless for differentiation; (*b*) the m. p.s of many of their derivatives are markedly affected by the extent and rate of heating, and a statement of m. p. without that of temperature of immersion may be misleading; (c) several pairs of corresponding salts have almost identical m. p.s, which are not always depressed on admixture. For rapid reference, the Table gives the m. p.s, under the conditions specified in the Experimental section, of an extensive comparable series of derivatives of each of the above four amines.

M. p.s of derivatives of triethylenediamine (I); 1 : 2-*di*-(4-*methyl*-1-*piperazinyl*)*ethane* (XIII), 1 : 4-*dimethylpiperazine, and* 1-2′-*dimethylaminoethyl*-4-*methylpiperazine* (VIII).

	(I)	(XIII)	Dimethylpiperazine	(VIII)
Base : b. p.	(Sublimes)	91°/0·03 mm.	131—132°	94°/12 mm.
m. p.	156—157°	40—43°	—	—
Hydrochloride	320	286—288	265°	262°
Hydrobromide	360	267	244	239
Hydriodide	>360 [a]	231 [b]	237	266 [c]
Methobromide	296	296 [d]	364 [e]	315 [f]
Methiodide	284	288,[f] 270 [d]	334 [g]	320 [f]
Methopicrate	324	212 [d]	320	220 [f]
p-Nitrophenoxide	182—183	184	125—126	139
2 : 4-Dinitrophenoxide	158	221	216	165
Picrate	290	292	300	254
Nitrate	176	245	210	164
Oxalate	290	239—240	276	228
Chloroplatinate	324	287	282	242

[a] Chars without melting. [b] Trihydriodide. [c] Dihydriodide. [d] Triquaternary salt. [e] In evacuated tube. [f] Diquaternary salt. [g] In sealed tube.

It will be seen that the following pairs of salts have almost identical m. p.s: (i) the hydrochlorides of dimethylpiperazine and of the triamine (VIII); (ii) the *p*-nitrophenoxides of the amines (I) and (XIII); (iii) the picrates of (I) and (XIII); (iv) the chloroplatinates of (XIII) and dimethylpiperazine: mixtures of the components of each of these pairs show depression of m. p. On the other hand, mixtures of the dimethopicrates of (I) and of dimethylpiperazine do not show a depression, nor do those of the dihydrobromides of (I) and of piperazine.

As examples of possible misdirection due to identification by m. p.s, McElvain and Bannister [6] state that the thermal decomposition of 1-2′-bromoethylpiperazine gives triethylenediamine, identified as its (unanalysed) di-*p*-nitrophenoxide, m. p. 182·5—183·5°, and hexaethylenetetramine, identified as its tetrapicrate, m. p. 275° (decomp.). The former m. p. clearly does not differentiate between the amines (I) and (XIII). The m. p. of the picrate is very close to that given for hexaethylenetetramine tetrapicrate (277°) by Mann and Mukherjee,[1] but we have found that some salts in this series, more particularly the picrates, when prepared from thermal decomposition products, give satisfactory analytical values after repeated recrystallisation, although the m. p. has meanwhile

[6] McElvain and Bannister, *J. Amer. Chem. Soc.*, 1954, **76**, 1126.

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risen to a constant but low value (for other examples, see p. 1890), and the true m. p. can be obtained only from the salt prepared from the pure base. Consequently the identity of McElvain and Bannister's picrate also remains uncertain. The method of preparation virtually precludes its being the picrate of the methylated amine (XIII) : it might possibly be the dipicrate of the apparently unknown vinylpiperazine.

Schwarzenbach *et al.*[7] decomposed a salt, stated to be the chloride monohydrochloride corresponding to the salt (VI), and fractionally extracted the picrates of the crude product, as Mann and Mukherjee [1] describe. The hydrochloride obtained from the more soluble picrate was extensively purified and then had m. p. 290°; it was not analysed, but converted into a diperchlorate, which analysis showed was hydrated. The hydrochloride was considered to be that of the amine (I), but we find this salt to be a highly deliquescent compound, m. p. 320° (lit.,[2] 310—311°) whereas the non-hygroscopic tetrahydrochloride of the amine (XIII) has m. p. 286—288°. Hromatka [3] describes the perchlorate of the amine (I) without analysis or m. p.

The therapeutic properties of triethylenediamine (I) have been kindly investigated by Imperial Chemical (Pharmaceuticals) Ltd., who report: "Because of the chemical relationship of triethylenediamine to piperazine, it was studied against an infection of of *Heterakis spumosa* in mice. It showed no activity at doses of 1·25 g./kg. given three times. Piperazine would have been fully active at this dose level. The diamine (I) produced no marked pharmacological effects in the cat, apart from a transient decrease in blood pressure.

"The diamine (I) is also without action in cotton rats infected with *Litomosoides carinii* at a dose of 4 × 250 mg./kg. There are 1 : 4-disubstituted piperazines which show activity against this infection, although piperazine is without effect."

Mr. O. D. Standen, of the Wellcome Laboratories of Tropical Medicine, has kindly investigated the value of the chloride dihydrochloride (VI) and the trihydrochloride (VII) as possible schistosomicides, and finds that they are inactive.

Experimental

All compounds were colourless unless otherwise described. The m. p.s of most compounds were dependent on the temperature of immersion, which is indicated as (T.I. −°) immediately after the recorded m. p. Many compounds were almost insoluble in boiling methanol or ethanol, but readily dissolved when water was cautiously added dropwise to the boiling suspension, and would then crystallise on cooling: the approximate dilution by water is indicated as, for example, 95% ethanol when 5% (by wt.) of water has thus been added.

1-2′-*Chloroethyl*-4 : 4-*dimethylpiperazinium Chloride Monohydrochloride* (III).—(i) The clear solution obtained by the addition of trichlorotriethylamine hydrochloride (7·5 g.) to a 40% (w/v) solution of methanolic dimethylamine (12 c.c.; 3·4 mols. of amine) was heated in a sealed tube at 45—50° for 1·5 hr. The cold solution, containing a very small amount of crystalline material, was cooled to 0° whilst being saturated with hydrogen chloride, and the resulting clear solution was evaporated to dryness in a vacuum desiccator. The pale brown residue, when recrystallised first from ethanol to remove a trace of insoluble material, then from ethanol containing 2—3 drops of concentrated hydrochloric acid, and again from ethanol, furnished the *monohydrate* (1·7 g.) of the monohydrochloride (III) (Found: C, 36·1; H, 8·1; N, 10·5; Cl, 39·4. $C_8H_{18}N_2Cl_2,HCl,H_2O$ requires C, 35·9; H, 7·9; N, 10·5; 3Cl, 39·7%), which when heated at 110°/0·1 mm. for 4 hr. gave the anhydrous salt (Found: C, 38·5; H, 7·8; N, 11·1. Calc. for $C_8H_{18}N_2Cl_2,HCl$: C, 38·5; H, 7·7; N, 11·3%). The behaviour of the monohydrate on heating is characteristic: (*a*) immersed at 150°, the hydrate effervesced at 245—250° to form a gum which appeared to solidify and then melted with gentle effervescence at 263—264°; (*b*) immersed at 160°, gentle effervescence with shrinking immediately occurred, and the behaviour then followed (*a*); (*c*) immersed at 250°, it underwent a slight brief effervescence at 254—255° and melted with vigorous effervescence at 264°. The anhydrous salt behaved as in (*c*).

Aqueous solutions of the monohydrochloride (III) and picric acid when mixed deposited

[7] Schwarzenbach, Maissen, and Ackermann, *Helv. Chim. Acta*, 1952, **35**, 2333.

a picrate, m. p. 196—198° (decomp.) (T.I. 180°), which when twice recrystallised from water underwent complete hydrolysis to the chlorine-free 1-2′-*hydroxyethyl*-4 : 4-*dimethylpiperazinium dipicrate*, yellow crystals, m. p. 220° (decomp.) (T.I. 200°) (Found : C, 38·85; H, 3·9; N, 17·6. $C_{20}H_{24}O_{15}N_8$ requires C, 38·95, H, 3·9; N, 18·2%). This compound, being unaffected in m. p. and composition by being heated at 70°/0·1 mm. for 6 hr. (Found : C, 38·55; H, 3·8%), is unlikely to be the monohydrated vinyl derivative.

A methanolic solution of the monohydrochloride (III) was shaken with silver oxide and filtered. One portion of the filtrate was diluted with methyl iodide and set aside for 24 hr., crystals slowly separating. These were soluble in cold methanol, but when thrice recrystallised from 98% ethanol furnished 1-2′-*chloroethyl*-4 : 4-*dimethylpiperazinium iodide* (IV), m. p. 236° (decomp.) (T.I. 230°) (Found : C, 31·6; H, 5·9; N, 9·0. $C_8H_{18}N_2ClI$ requires C, 31·5; H, 6·0; N, 9·2%). This salt, heated (*a*) rapidly from room temperature, (*b*) more slowly, had m. p. 246° (decomp.) and 265—270° (decomp.) respectively. A second portion of the filtrate, similarly diluted, boiled under reflux for 2 hr., then concentrated and taken to dryness in a vacuum, gave a residue which, recrystallised as before, afforded the 1-2′-*chloroethyl*-1 : 4 : 4-*trimethylpiperazinium di-iodide* (V), m. p. 182° (decomp.) (T.I. 170°) (Found : C, 24·2; H, 4·35. $C_9H_{21}N_2ClI_2$ requires C, 24·2; H, 4·7%).

(ii) Experiments similar to (i) were carried out with the 40% methanolic dimethylamine solution (2·0, 2·7, and 6·6 mols.) with heating as before, and with the dimethylamine (3·4 mols.), the solution in this experiment being set aside at room temperature for 24 hr. : all these conditions furnished the above monohydrate (Found, using 2·7 mols. of amine at 45° : C, 36·0; H, 8·0% : using 3·4 mols. of amine at room temperature : C, 36·2; H, 7·8; N, 10·5%).

(iii) The solution, prepared as in (i), was heated at 45—50° for 4 hr. The dry product was extracted with boiling ethanol, leaving a very small residue, which, recrystallised from 95% ethanol, gave crystals, m. p. 316° (decomp.) (T.I. 300°) which appeared to be 1-2′-chloroethyl-4 : 4-dimethylpiperazinium chloride monohydrate (Found : C, 41·8; H, 8·3; N, 12·2. $C_8H_{18}N_2Cl_2,H_2O$ requires C, 41·6; H, 8·7; N, 12·1%). An aqueous solution, treated with aqueous picric acid and sodium picrate, gave a picrate, yellow crystals, m. p. 290° (vigorous decomp.) (T.I. 280°), after recrystallisation from water, whereas the above salt should have given the picrate, m. p. 220°, described above. Insufficient material precluded decisive identification.

The residue from the evaporation of the ethanolic extract, recrystallised as in (i), gave the hydrated hydrochloride (III).

(iv) The solution, prepared as in (i), was heated at 45—50° for 2 hr. When an ethanolic solution of the crude dry product was treated with a small quantity of ethanolic hydrogen chloride, a cream-coloured powder separated during 36 hr. This product, m. p. 216° (decomp.) (T.I. 200°), although approximating in composition to the monohydrated monohydrochloride (III), was a mixture, and two recrystallisations from ethanol containing hydrochloric acid gave a white powder, m. p. 226° (effervescence) (T.I. 210°), which was still impure (Found : C, 35·8; H, 8·2; N, 11·6; Cl, 38·2%). Repeated and wasteful crystallisation from ethanol ultimately gave the hydrated monochloride (III). If however the cream-coloured powder was collected after only 16—18 hr., a second constituent could be isolated by repeated dissolution in ethanol followed by addition of sufficient ethanolic hydrogen chloride to cause crystallisation, giving a highly deliquescent *compound* of m. p. 290° (effervescence) (T.I. 280°) in very small yield (Found : C, 42·1; H, 8·4; N, 13·8; Cl, 35·2. $C_7H_{16}N_2Cl_2$ requires C, 42·2; H, 8·1; N, 14·1; Cl, 35·6%). A cold methanolic solution of this salt, when shaken with silver oxide, filtered, and treated with methyl iodide, rapidly deposited crystals, m. p. 304—305° (T.I. 280°) which when twice recrystallised from 80% methanol had m. p. 310° (decomp.) (T.I. 300°) (Found : C, 29·75; H, 5·9; N, 9·9%) and when then thrice recrystallised from 80% ethanol had the same m. p. (Found, after drying at 60°/0·1 mm. for 7 hr. : C, 30·25; H, 5·8; N, 9·7. $C_7H_{16}N_2ClI$ requires C, 29·0; H, 5·5; N, 9·65%). A solution of this *methiodide* in hot 90% methanol, when diluted with methyl iodide, boiled under reflux for 2 hr. and evaporated, gave apparently the unchanged methiodide, m. p. 308—310° (decomp.) (T.I. 295°) after two recrystallisations from 80% methanol (Found : C, 30·2; H, 6·0; N, 9·4%). The identity of the chloride of m. p. 290° remains uncertain : it cannot be 1-2′-chloroethyl-4-methylpiperazine hydrochloride or triethylenediamine hydrochloride methochloride, for the first compound, treated as above in the cold, would give the methiodide (IV), m. p. 236°, and the second would give triethylenediamine dimethiodide, m. p. 284° (cf. p. 1891).

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Mann and Mukherjee [1] record m. p. 218° for the monohydrochloride (III) and m. p. 302—305° for its methiodide: it is probable that their recrystallised monohydrochloride was analogous to the above impure product, m. p. 226°, and that it also furnished the above methiodide.

1-2′-*Dimethylaminoethyl*-4-*methylpiperazine* (VIII). *Preparation of the Trihydrochloride* (VII).—A freshly prepared mixture of 2 : 2′ : 2″-trichlorotriethylamine monohydrochloride (50 g.) and a 40% (w/v) methanolic solution of dimethylamine (250 c.c.; 10·7 mols. of amine) was electrically stirred in an autoclave at 125° for 7 hr. The cold partly crystalline liquid was transferred to a beaker and thoroughly chilled, whilst saturated with hydrogen chloride: during this process, it initially became a clear liquid, which then deposited crystals. The crystals, when collected, washed with methanol, and recrystallised twice from methanol, gave the trihydrochloride (VII) (47 g.), m. p. 262° (Found: C, 38·6; H, 8·7; N, 15·2; Cl^-, 37·5. Calc. for $C_9H_{21}N_3,3HCl$: C, 38·5; H, 8·6; N, 15·0; Cl, 37·9%). A mixture of this salt with dimethylpiperazine dihydrochloride had m. p. 240—242° (decomp.) (T.I. 230°).

Very many successful runs were carried out using the above conditions: however, on one occasion a leak in the top of the autoclave released much dimethylamine vapour, and this run furnished solely the dihydrochloride (VI). Mann and Mukherjee's experiments [1] were carried out in a rotating autoclave, in which the sealing, temperature, and rotation were difficult to adjust satisfactorily, and this may have accounted for isolation of the salt (VI) apparently under the above conditions.

The hydrochloride (VII) (20 g.) was decomposed with concentrated aqueous potassium hydroxide, and the liberated *base* (VIII), after extraction with ether and further drying (KOH), was obtained as a colourless, almost odourless liquid, b. p. 94°/12 mm., freely soluble in water (Found: C, 63·3; H, 12·4%; *M*, cryoscopic in benzene, 167. $C_9H_{21}N_3$ requires C, 63·1; H, 12·4%; *M*, 171).

The following derivatives were prepared from the base or its hydrochloride for decisive characterisation.

A solution of the hydrochloride in aqueous methanol was shaken with silver oxide, filtered, treated with concentrated hydrobromic acid, again filtered, and evaporated in a desiccator. The syrupy residue when rubbed with ethanol gave the crystalline *trihydrobromide*, m. p. 238—239° (decomp. with effervescence) (T.I. 225°) after crystallisation from ethanol (Found: C, 26·0; H, 6·2; N, 10·2. $C_9H_{21}N_3,3HBr$ requires C, 26·1; H, 5·85; N, 10·15%). An ethanolic solution of the base was added to an excess of chilled, stirred hydriodic acid (of constant b. p.); the precipitated crystals, when twice recrystallised from 95% ethanol, gave the *dihydriodide*, m. p. 266° (decomp.) (T.I. 250°) (Found: C, 25·5; H, 5·5; N, 9·9. $C_9H_{21}N_3,2HI$ requires C, 25·3; H, 5·4; N, 9·8%).

A methanolic solution of the base, diluted with methyl bromide and set aside for 3 hr., gave heavy crystals of the *dimethobromide* (IX; X = Br), m. p. 315° (effervescence) (T.I. 300°) after crystallisation from methanol (Found: C, 36·65; H, 7·3; N, 11·85. $C_{11}H_{27}N_3Br_2$ requires C, 36·6; H, 7·5; N, 11·7%). A methanolic solution of the base, diluted with methyl iodide and set aside for 16 hr., deposited the dimethiodide (IX; X = I), which when recrystallised from 98% methanol, formed a *dimethanolate*, m. p. 320° (effervescence) (T.I. 310°) (Found: C, 29·6; H, 6·5; N, 8·9. $C_{11}H_{27}N_3I_2,2CH_4O$ requires C, 29·6; H, 6·4; N, 8·6%); heating at 75°/0·1 mm., for 6 hr. gave the solvent-free *salt* of unchanged m. p. (Found: C, 29·2; H, 6·05; N, 9·1. $C_{11}H_{27}N_3I_2$ requires C, 29·0; H, 6·0; N, 9·2%). The m. p. of this salt is markedly affected by the rate of heating. When the above solution containing methyl iodide was refluxed for 1 hr., the same product was obtained. The addition of an aqueous solution of this salt to aqueous sodium picrate deposited the *dimethopicrate*, deep orange crystals, m. p. 220° (decomp.) (T.I. 210°) from methanol (Found: C, 42·5; H, 4·5; N, 19·2. $C_{23}H_{31}O_{14}N_9$ requires C, 42·0; H, 4·75; N, 19·4%).

When ethereal solutions of the base and an excess of *p*-nitrophenol were mixed, the tri-*p*-nitrophenoxide was immediately deposited, and formed bright yellow crystals, m. p. 139° (T.I. 130° or from room temperature), from ethanol (Found: C, 55·4; H, 6·5. Calc. for $C_9H_{21}N_3,3C_6H_5O_3N$: C, 55·1; H, 6·2%). Hromatka and Kraupp [2] give m. p. 142—142·5°. The *tri*-2 : 4-*dinitrophenoxide*, similarly prepared, formed orange plates, m. p. 164—165° (T.I. 160°), after crystallisation from ethanol (Found: C, 44·65; H, 4·4; N, 17·3. $C_9H_{21}N_3,3C_6H_4O_5N_2$ requires C, 44·8; H, 4·6; N, 17·4%). Hromatka and Kraupp [2] mention this compound without analytical identification.

The base in aqueous solution gave a yellow *tripicrate*, m. p. 254° (decomp.) (T.I. 240° and 250°) after crystallisation from water (Found: C, 37·85; H, 3·4; N, 19·75. $C_9H_{21}N_3,3C_6H_3O_7N_3$ requires C, 37·75; H, 3·5; N, 19·6%).

An aqueous solution of the base when added (i) to dilute nitric acid deposited the *trinitrate*, m. p. 164° (vigorous decomp.) (T.I. 150°) (Found: C, 30·1; H, 6·8; N, 22·85. $C_9H_{21}N_3,3HNO_3$ requires C, 30·0; H, 6·7; N, 23·3%), and (ii) to saturated aqueous oxalic acid slowly deposited the *tri*(*hydrogen oxalate*), m. p. 228° (decomp.) (T.I. 220°) (Found: C, 41·0; H, 6·4; N, 9·25. $C_9H_{21}N_3,3C_2H_2O_4$ requires C, 40·8; H, 6·2; N, 9·5%). The hydrochloride gave a *chloroplatinate*, orange crystals, m. p. 242° (decomp. with effervescence) (T.I. 230°) (Found: C, 13·6; H, 3·45; N, 5·6. $2C_9H_{21}N_3,3H_2PtCl_6$ requires C, 13·7; H, 3·0; N, 5·3%). The nitrate and oxalate recrystallised from aqueous ethanol and the chloroplatinate rapidly from water.

1-2′-*Dimethylaminoethyl*-4 : 4-*dimethylpiperazinium Chloride Dihydrochloride* (VI).—This preparation was most conveniently carried out in pressure-bottles, having rubber stoppers wired in place. A mixture of trichlorotriethylamine hydrochloride (10 g.) and 40% (w/v) methanolic dimethylamine (60 c.c.; 12·8 mols. of amine) was thus heated in a water-bath at 45—50° for 8 hr. The united liquid products from five such experiments were then chilled and saturated with hydrogen chloride. The precipitated salt, when twice recrystallised from 97% ethanol, gave the dihydrochloride (VI) as the monohydrate (58 g.), m. p. 228° (effervescence) (Found: C, 38·6; H, 8·75; N, 13·4. Calc. for $C_{10}H_{24}N_3Cl,2HCl,H_2O$: C, 38·4; H, 9·0; N, 13·4%), which when confined in a vacuum over phosphoric anhydride for several days gave the anhydrous salt of unchanged m. p. (lit.,[7] m. p. 225°) (Found: C, 40·9; H, 9·2; N, 13·7; Cl, 35·8. Calc. for $C_{10}H_{24}N_3Cl,2HCl$: C, 40·7; H, 8·9; N, 14·2; Cl, 36·1%). The salt is only sparingly soluble in boiling absolute ethanol.

The chloride dihydrochloride (VI) gave the following derivatives. An aqueous solution of the salt, when shaken with silver oxide, filtered, acidified with hydrobromic acid, and evaporated to dryness in a desiccator, gave the very hygroscopic *bromide dihydrobromide*, m. p. 270° (effervescence) (T.I. 260°) after crystallisation from ethanol (Found: C, 34·0; H, 7·5; N, 11·8. $C_{10}H_{24}N_3Br,2HBr$ requires C, 34·6; H, 7·3; N, 12·1%). A methanolic solution of the salt (VI), when treated in turn with silver oxide and methyl bromide, gave a salt (IX ; X = Br) identical with the dimethobromide of the base (VIII), m. p. 315° (effervescence) (T.I. 300°) after crystallisation from methanol (Found: C, 36·15; H, 8·2; N, 11·4%), and with methyl iodide gave the dimethiodide (IX ; X = I), m. p. 317° (effervescence) (T.I. 310°) (Found, after heating at 75°/0·1 mm. for 7 hr.: C, 29·1; H, 6·0; N, 9·4%).

The salt (VI) also gave a *tripicrate*, yellow crystals, m. p. 218—220° (decomp.) (T.I. 215°) after crystallisation from aqueous ethanol (Found: C, 38·7; H, 3·9; N, 19·4. $C_{16}H_{28}O_7N_6,2C_6H_3O_7N_3$ requires C, 38·5; H, 3·7; N, 19·25%), and a *chloroplatinate*, orange crystals, m. p. 248° (decomp.) (T.I. 240°), after crystallisation from water [Found: C, 15·3; H, 3·4; N, 5·4. $(C_{10}H_{26}N_3)_2(PtCl_6)_3$ requires C, 15·0; H, 3·3; N, 5·15%].

Triethylenediamine (I).—***Preparation.*** Because only comparatively small quantities of this base can be prepared in one operation, it was most convenient to insert pure powdered triethylenediamine dimethobromide (2 g.) into the glass tube *A* (through a paper cylinder temporarily inserted to ensure complete absence of the salt from the upper part of *A*), then to cover the salt with a plug of glass wool *B* to prevent the fine solid particles being subsequently thrown upwards, and finally to seal the top of *A*. The side-arm was then fitted by a ground-glass joint *C* into the receiver *D–E*, joints being covered with a " high temperature vacuum " lubricant. The receiver *E* was immersed in carbon dioxide–acetone, the apparatus evacuated to 0·003 mm., and the vessel *A* then heated in a Silicone bath to 230—240°. In 4—5 hr., crystals of the base (0·6 g., 81%) slowly formed, almost exclusively in zone *F* of the central tube, a fine sandy residue (0·6 g.) remaining in *A*. Repetition of this experiment, using (*a*) the dimethobromide (3 g.) and the above conditions, (*b*) the bromide (4 g.) with heating extended to 7 hr., gave yields of the crystalline base of 0·66 g. (59%) and 0·85 g. (57%) respectively: a series of short runs with the dimethobromide (2 g.) was thus found to be most effective. The base (I) so obtained contained a trace of bromide, but when resublimed from a similar apparatus gave the pure base, m. p. 156—157° (in a sealed tube, from room temperature) when thoroughly dried in a vacuum (KOH) (Found: C, 64·1; H, 11·1; N, 24·75; *M*, ebullioscopic in ethanol, 112; in benzene, 120. Calc. for $C_6H_{12}N_2$: C, 64·2; H, 10·8; N, 25·0%; *M*, 112).

Although the period of heating in the above experiment was continued until no further increase in the sublimed crystals was detected, the residue in *A* apparently still contained

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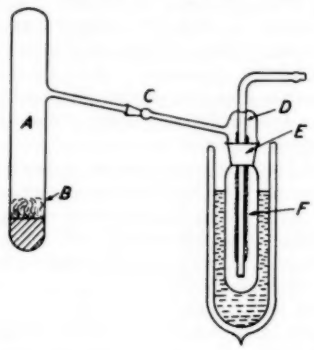
unchanged dimethobromide. A sample of this residue was dissolved in cold 48% w/w hydrobromic acid, filtered to remove a trace of insoluble material, and diluted with ethanol. The fine crystalline deposit, when thrice recrystallised from methanol–ethanol and dried at 50°/0·01 mm., gave the dimethobromide, m. p. 285—286° (decomp.) (T.I. 280°) (Found: C, 32·1; H, 6·3; N, 9·3. Calc. for $C_8H_{18}N_2Br_2$: C, 31·8; H, 6·0; N, 9·3%). A methanolic solution of this product, when added to an acetone solution of sodium iodide, deposited the dimethiodide,



m. p. 270° (decomp.) (T.I. 260°) (Found: C, 24·4; H, 4·6; N, 7·3. Calc. for $C_8H_{18}N_2I_2$: C, 24·3; H, 4·6; N, 7·1%). The m. p.s of these two compounds, compared with those of the authentic salts described below, indicate that, in spite of the analytical values, they still were not quite pure.

In the hope of reducing the time required for the preparation of the diamine, a number of experiments were performed in which the thermal decomposition was carried out at a much higher temperature: the receiver *D–E* was now duplicated in series to enable different condensation temperatures to be employed. In no case was the free diamine (I) thus obtained. As examples, the dimethobromide (2 g.) was heated in *A* at 300°/0·002 mm., the temperature rising to 350° during 30 min. The first receiver, cooled in water at 15°, remained empty. The second receiver, cooled in liquid oxygen, collected a white semi-solid product, which was allowed to attain room temperature whilst still in the vacuum, a volatile liquid, presumably methyl bromide, boiling off as slight " crackling " of the product indicated possible reconversion. This product was dissolved in hydrobromic acid and evaporated to dryness: the residue, thrice recrystallised from methanol and dried at 50°/0·1 mm., afforded apparently *triethylenediamine hydrobromide methobromide* (X; X = Br), m. p. 286° (effervescence) (T.I. 275°) (Found: C, 29·0; H, 5·1; N, 9·3. $C_7H_{15}N_2Br,HBr$ requires C, 29·2; H, 5·6; N, 9·7%). The residue in *A* was extracted with boiling methanol, which on cooling gave a pale brown deposit, furnishing piperazine dihydrobromide, m. p. 360° (decomp.) (T.I. 354°) after repeated crystallisation from 95% methanol (Found: C, 19·1; H, 4·95%).

An authentic sample of this salt was prepared by dissolving pure piperazine in 48% hydrobromic acid, which rapidly deposited dense crystals: these were almost insoluble in boiling absolute methanol and ethanol, but when recrystallised from aqueous ethanol furnished the dihydrobromide, heavy needles, m. p. 360° (decomp.) (T.I. 300°) (Found: C, 19·5; H, 4·9. Calc. for $C_4H_{10}N_2,2HBr$: C, 19·4; H, 4·9%).

In another experiment, the dimethobromide (8 g.) was heated gently at first and then strongly with a " brush " flame, a dark brown liquid ultimately collecting in the first receiver. This liquid, when evaporated with hydrobromic acid, gave a very impure product, which after seven recrystallisations from ethanol–methanol furnished 1 : 4-dimethylpiperazine dihydrobromide, m. p. 240—241° (T.I. 230°) (Found: C, 26·2; H, 5·5. Calc. for $C_6H_{14}N_2,2HBr$: C, 26·1 ; H, 5·8%). The product in the second receiver was insufficient for purification and identification.

The diamine (I) is soluble in cold water, methanol, ethanol, ether, and benzene: it can be recrystallised from *cyclo*hexane and from light petroleum (b. p. 60—80°), but the crystals when contaminated with these solvents become exceedingly volatile in a vacuum, and direct sublimation affords a more rapid amd effective purification.

Derivatives. An ethanolic solution of the base, when added to chilled concentrated hydrochloric acid, deposited crystals; the clear solution, obtained by warming this mixture, on cooling deposited the dihydrochloride as long very deliquescent needles, m. p. 320° (decomp.) (T.I. 310°) (Found : N, 15·5. Calc. for $C_6H_{12}N_2,2HCl$: N, 15·4%). Hromatka and Kraupp [2] give m. p. 310—311°. A concentrated solution of the base in 48% hydrobromic acid, when diluted with ethanol, gave the *dihydrobromide*, m. p. 360° (decomp.) (T.I. 350°), after crystallisation from aqueous ethanol (Found : C, 26·45; H, 5·4; N, 10·3. $C_6H_{12}N_2,2HBr$ requires C, 26·3; H, 5·15; N, 10·2%). A mixture of this salt and piperazine dihydrobromide, carefully dried, also had m. p. 360° (decomp.) (T.I. 330°) with some preliminary softening.

The *dihydriodide*, prepared as the dihydrochloride, and recrystallised from ethanol, charred with melting from *ca.* 360° upwards (Found : C, 19·6; H, 4·0; N, 7·6. $C_6H_{12}N_2,2HI$ requires C, 19·6; H, 3·8; N, 7·6%); when exposed to daylight at room temperature it remained colourless for several days.

The *dimethochloride* was prepared by heating a methanolic solution of the base and an excess of methyl chloride in a sealed tube at 55—60° for 2 hr.; after cautious removal of the unused methyl chloride, evaporation gave a white residue of the dimethochloride, which, after two recrystallisations from ethanol, still formed exceedingly deliquescent crystals, m. p. 284° (decomp.) (T.I. 140°, 260°, the samples being thoroughly dried in the capillary tubes, which were then sealed) (Found : C, 44·5; H, 8·8; N, 12·6. $C_8H_{18}N_2Cl_2$ requires C, 45·1; H, 8·5; N, 13·1%). Alternatively, a methanolic solution of the dimethiodide (see below), mixed with an excess of silver chloride, was boiled for 1 hr. and filtered : the filtrate evaporated without residue. The silver halide was extracted with boiling 85% methanol, which on filtration and evaporation gave the dimethochloride, having identical m. p. after crystallisation.

The dimethobromide, prepared in cold methanol, recrystallised from 98% ethanol and dried (P_2O_5), had m. p. 296° (T.I. 290°), unchanged by admixture with the salt obtained by combining 1 : 4-dimethylpiperazine and ethylene dibromide (Found : C, 31·7; H, 5·9; N, 9·1%; *M*, cryoscopic in 0·5981% aqueous solution, 101; in 0·7729%, 100; in 1·037%, 105. Calc. for $C_8H_{18}N_2Br_2$: C, 31·8; H, 6·0; N, 9·3%; *M*, 302). These molecular weight values, determined by Dr. A. Senior, confirm those of Mann and Mukherjee,[1] and indicate complete ionisation at these concentrations.

The dimethiodide, similarly prepared and recrystallised from methanol, had m. p. 284° (decomp.) (T.I. 276°) (Found : C, 24·5; H, 4·8; N, 6·85. Calc. for $C_8H_{18}N_2I_2$: C, 24·3; H, 4·6; N, 7·1%). Hromatka and Engel [3] do not record a m. p. The *dimethopicrate*, prepared from the bromide and recrystallised from much water, formed deep yellow needles, m. p. 324—325° (effervescence) (T.I. 310°) (Found : C, 40·2; H, 3·9. $C_{20}H_{22}O_{14}N_8$ requires C, 40·15; H, 3·7%).

The di-*p*-nitrophenoxide, prepared in ether and recrystallised from ethanol, formed deep yellow crystals, m. p. 182—183° (T.I. 20° or 170°) (Found : C, 55·5; H, 6·3; N, 14·3. Calc. for $C_6H_{12}N_2,2C_6H_5O_3N$: C, 55·4; H, 5·7; N, 14·35%). Solutions of this salt in ethanol and in boiling ether are pale yellow and colourless respectively, the salt apparently undergoing complete dissociation in ether. The di-2 : 4-dinitrophenoxide, prepared in benzene and recrystallised from ethanol, formed yellow crystals, m. p. 158° (T.I. 145°) (Found : C, 45·3; H, 4·5; N, 17·3. Calc. for $C_6H_{12}N_2,2C_6H_4O_5N_2$: C, 45·0; H, 4·2; N, 17·5%). The dipicrate, prepared in ethanol and recrystallised from water, formed pale yellow crystals, m. p. 290° (moderately vigorous decomp.) (T.I. 285°) (Found : C, 38·05; H, 3·4; N, 20·1. Calc. for $C_6H_{12}N_2,2C_6H_3O_7N_3$: C, 37·9; H, 3·2; N, 19·6%). Hromatka [2,3] states that these compounds melt at 183°, 159°, and " not below 280° " respectively.

The *dinitrate* separated as fine needles, m. p. 176° (decomp.) (T.I. 165°), when the base in ethanol was added to moderately dilute nitric acid (Found : C, 30·2; H, 5·7; N, 23·2. $C_6H_{12}N_2,2HNO_3$ requires C, 30·25; H, 5·9; N, 23·5%). The di(hydrogen oxalate) readily crystallised when ethanolic solutions of the base and oxalic acid were mixed. After crystallisation from 95% ethanol and drying (P_2O_5), it had m. p. 290° (decomp.) (open tube, T.I. 220°), 270° (decomp.) (evacuated tube, T.I. 240°), and when heated rapidly from room temperature decrepitated at *ca.* 200°, softened at *ca.* 280°, and melted at 287° (decomp.), the value given by Hromatka [3] (Found : C, 40·7; H, 5·6; N, 9·3. Calc. for $C_6H_{12}N_2,2C_2O_4H_2$: C, 41·1; H, 5·5; N, 9·6%). The *chloroplatinate*, prepared from the base and an excess of chloroplatinic acid, each in 20% hydrochloric acid, formed orange crystals, m. p. 324° (decomp., preliminary

[3] Hromatka and Engel, *Ber.*, 1943, **76**, 713.

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darkening) (T.I. 310°) (Found: C, 14·1; H, 2·7; N, 5·5; Pt, 37·5. $C_6H_{12}N_2,H_2PtCl_6$ requires C, 13·8; H, 2·7; N, 5·4; Pt, 37·4%).

The volatility of triethylenediamine can be further assessed from the following experiments. (i) The weight of the powdered amine (0·0968 g.), confined at room temperature in an atmospheric desiccator (1·6 l.) containing paraffin wax shavings and sodium hydroxide pellets, fell to 0·0778, 0·0718, and 0·0708 g. after 2, 5, and 7 days respectively. (ii) The weight of the amine (0·1098 g.), similarly confined in this desiccator at 15 mm., over sodium hydroxide alone, was 0·0218 and 0·0058 after 3 and 5 days respectively: sublimation was complete after 6 days. (iii) The base (0·100 g.) slowly volatilised in the air at room temperature; after 2 days the powdered material had formed a glass, which completely volatilised in 8 days. (iv) A solution of the base (0·2 g.) in dry ether (30 c.c.) in an all-glass apparatus was very slowly distilled (from a Silicone bath) into a receiver closed by a calcium chloride tube. The distillate gave only a faint turbidity with ethanolic picric acid, and crystalline base remained in the distillation flask. (v) Solutions of (*a*) the base (0·1200 g.) in ethanol (20 c.c.), and (*b*) the base (0·116 g.) in benzene (20 c.c.), were similarly distilled during 1·5 hr. The distillate, when treated in (*a*) with aqueous picric acid, and in (*b*) with ethanolic picric acid, gave a suspension of the picrate too fine for adequate filtration and weighing. The residue in the distillation flasks, when dissolved in water and treated with aqueous picric acid, deposited the amine dipicrate (0·240 and 0·3610 g.) indicating a recovery of 39 and 61% respectively of the base. The dipicrate has a low solubility in cold water, and these figures give a reasonably accurate assessment of the volatility of the base.

The base has considerable stability to acids. A solution of the base (0·3 g.) in 48% w/v hydrobromic acid (5 c.c.), when boiled under reflux for 2 hr., concentrated, and cooled, deposited long needles of the dihydrobromide, m. p 355—357° (decomp.) (T.I. 350°) after recrystallisation from aqueous ethanol, of the base (Found: C, 25·8; H, 4·9; N, 9·6%). The filtrate from the needles was basified and extracted with ether: the extract, when boiled with methanolic methyl iodide, gave the dimethiodide, m. p. and mixed m. p. 281—283° (decomp.) (T.I. 275°). The stability of the base to sulphuric and nitric acids has been noted by Hromatka.[3]

1:4-Dimethylpiperazine, b. p. 131—132°, prepared by Mann and Senior's method,[5] gave the following derivatives, recorded here for comparison with those obtained from thermal decomposition products described later. Certain of these compounds have been recorded by Mann and Senior, who usually gave the m. p. when the compound was heated from room temperature.

The dihydrochloride, recrystallised from ethanol, has m. p. 265° (decomp., effervescence) (T.I. 235°, 250°) (Found: C, 38·4; H, 8·85; N, 14·75. Calc. for $C_6H_{14}N_2,2HCl$: C, 38·5; H, 8·6; N, 14·9%); in an evacuated tube, it had m. p. 241° (decomp. as before) (T.I. 220°) with decrepitation on immersion. The dihydrobromide, recrystallised from ethanol, had m. p. 244° (decomp.) (T.I. 230°) and, in an evacuated tube, m. p. 233° (decomp.) (T.I. 220°) (Found: C, 25·9; H, 5·6; N, 10·2. Calc. for $C_6H_{14}N_2,2HBr$: C, 26·1; H, 5·8; N, 10·15%).

The *dihydriodide* was precipitated when hydriodic acid (of constant b. p.) was cautiously added to a chilled ethanolic solution of the base; after crystallisation from 90% ethanol, it had m. p. 237° (decomp.) (T.I. 228°) (Found: C, 19·7; H, 4·2; N, 7·3. $C_6H_{14}N_2,2HI$ requires C, 19·45; H, 4·3; N, 7·6%).

A methanolic solution of the base was chilled, diluted with an excess of methyl chloride, sealed in a tube, and set aside for 20 hr. at room temperature. The clear solution was then exposed to the air to remove unused chloride, and evaporated to dryness in a desiccator. The residue, when recrystallised from ethanol–ether, gave the *monomethochloride*, very deliquescent crystals, which when immersed in a sealed tube at 330° effervesced, resolidified, and then sublimed with decomp. at 355° (Found: C, 51·3; H, 10·6; N, 17·0. $C_7H_{17}N_2Cl$ requires C, 51·05; H, 10·4; N, 17·0%). It is very soluble in methanol and ethanol. This experiment was repeated, but the sealed tube was heated at 55° for 5 hr. The considerable crystalline deposit, which separated on cooling, was collected and recrystallised from much methanol, giving the very slightly hygroscopic *dimethochloride*, which when immersed in a sealed tube at 350° sublimed at 360—365° with decomp. (Found: C, 44·9; H, 9·0; N, 12·8. $C_8H_{20}N_2Cl_2$ requires C, 44·7; H, 9·4; N, 13·0%).

The dimethobromide, prepared by the action of methyl bromide on the methanolic base at 60°, recrystallised from 95% ethanol and dried at 50°/0·1 mm., had m. p. 364° (decomp.) (evacuated tube, T.I. 350°); when it was immersed in an open tube at 360°, sublimation and

decomposition were complete by 375° (Found: C, 31·8; H, 6·4; N, 9·0. Calc. for $C_8H_{20}N_2Br_2$: C, 31·6; H, 6·6; N, 9·2%).

The dimethiodide, prepared by the interaction of methyl iodide and the base in cold methanol, and recrystallised from 30% v/v methanol, had m. p. 330°, 334° (decomp.) (T.I. 310°, 330°, both in sealed tubes); when it was heated in an open tube considerable sublimation occurred (Found: C, 24·0; H, 4·8; N, 7·2. Calc. for $C_8H_{20}N_2I_2$: C, 24·1; H, 5·0; N, 7·0%).

The pale yellow dimethopicrate, prepared from the aqueous methobromide and sodium picrate, and recrystallised from much water, had m. p. 320° (vigorous decomp.) (T.I. 290°) and in an evacuated tube, m. p. 310° (decomp.) (T.I. 280°, 300°) (Found: C, 40·0; H, 4·2; N, 18·6. Calc. for $C_{20}H_{24}O_{14}N_8$: C, 40·0; H, 4·0; N, 18·7%). It is insoluble in the usual organic solvents. A mixture of this salt and triethylenediamine dimethopicrate, m. p. 324—325°, had m. p. 320° (decomp.) (T.I. 290°): the two salts may be distinguished by the more vigorous (almost explosive) thermal decomposition of the former, and the darker and richer yellow colour of the latter.

The *di*-p-*nitrophenoxide*, prepared and recrystallised in ether, formed pale yellow crystals, m. p. 125—126° (Found: C, 55·0; H, 6·0; N, 14·1. $C_6H_{14}N_2,2C_6H_5O_3N$ requires C, 55·1; H, 6·2; N, 14·3%). It is readily soluble in water, methanol, ethanol, and acetone, but less so in ether and benzene.

The *di*-2 : 4-*dinitrophenoxide* separated, when ethereal solutions of the base and the phenol were mixed, as deep yellow crystals, m. p. 216° (decomp.) (T.I. 210°) after crystallisation from methanol (Found: C, 45·1; H, 4·6; N, 17·6. $C_6H_{14}N_2,2C_6H_4O_5N_2$ requires C, 44·8; H, 4·6; N, 17·4%).

The dipicrate, recrystallised from much water, formed yellow crystals, m. p. 300° (vigorous decomp.) (T.I. 295°); in an evacuated tube it explodes violently at 300° (T.I. 290°) (Found: C, 37·85; H, 3·55; N, 19·45. Calc. for $C_6H_{14}N_2,2C_6H_3O_7N_3$: C, 37·9; H, 3·2; N, 19·65%). It is almost insoluble in the common organic solvents.

The *dinitrate*, which readily separated when the base was added to concentrated nitric acid diluted with an equal volume of water, had m. p. 210° (moderately vigorous decomp.) (T.I. 200°) after crystallisation from 95% ethanol (Found: C, 30·3; H, 6·5; N, 23·2. $C_6H_{14}N_2,2HNO_3$ requires C, 30·0; H, 6·7; N, 23·3%).

The *di*(*hydrogen oxalate*) separated as a heavy crystalline deposit when concentrated ethanolic solutions of the base and acid were mixed; it had m. p. 276° (decomp.) (T.I. 270°) after crystallisation from 90% ethanol (Found: C, 40·7; H, 5·75; N, 9·0. $C_6H_{14}N_2,2C_2H_2O_4$ requires C, 40·8; H, 6·15; N, 9·5%).

The chloroplatinate, prepared in hydrochloric acid solutions of the base and acid, formed pale orange needles, m. p. 282° (effervescence) (T.I. 270°), unaffected by rapid recrystallisation from water (Found: C, 13·7; H, 2·9; N, 5·5; Pt, 37·3. Calc. for $C_6H_{14}N_2,H_2PtCl_6$: C, 13·75; H, 3·05; N, 5·35; Pt, 37·25%).

Thermal Decomposition of 1-2′-*Chloroethyl*-4 : 4-*dimethylpiperazinium Chloride Hydrochloride* (III).—The dry powdered monohydrate (0·9 g.), in a 25 c.c. conical flask to obtain a shallow layer and hence even heating, was immersed in a Silicone bath at 245—250° with stirring until effervescence ceased (5 min.). The cold pale amber glass was boiled with ethanol to which water was very cautiously added to give complete dissolution: the cold solution slowly deposited a microcrystalline powder, m. p. 280° (effervescence) (T.I. 270°). The united products from two such experiments, when twice so recrystallised, gave *triethylenediamine hydrochloride methochloride* (X; X = Cl), m. p. 288—289° (effervescence) (T.I. 280°) (Found: C, 42·3; H, 8·5; N, 14·1. $C_7H_{15}N_2Cl,HCl$ requires C, 42·2; H, 8·1; N, 14·1%): the salt is hygroscopic but undergoes deliquescence only very slowly.

A methanolic solution of the salt was shaken with silver oxide, filtered, diluted with methyl iodide, boiled under reflux for 1 hr., and cooled. The deposited crystals, m. p. 281—282° (T.I. 270°), when recrystallised from methanol gave triethylenediamine dimethiodide (Found: C, 24·5; H, 4·65%), m. p. 283—284° (decomp.) (T.I. 270°), unchanged by admixture with the authentic salt.

Synthesis of 1 : 2-*Di*-(4-*methyl*-1-*piperazinyl*)*ethane* (XIII).—The corresponding 4-ethoxycarbonyl derivative (XIV; R = CO_2Et) was prepared by the method of Stewart *et al.*[9] These

[9] Stewart, Turner, and Denton: Kushner, Brancone, McEwen, Hewitt, and Subbarow, *J. Org. Chem.*, 1948, **13**, 134.

workers extracted the ester (obtained as an oil in water) with ether. During this process the ester crystallises readily, probably as a hydrate, from the extract, even when copious quantities of ether are used. It was found advantageous therefore to stir the aqueous mixture until the oil solidified. It was then collected, washed with water, and dried. The combined filtrate and washing was twice extracted with ether, and the dried extract and the solid on distillation gave the pure ester, b. p. 165—168°/16 mm., in 81% yield.

The ester is only very slowly hydrolysed by boiling 20% hydrochloric acid. A mixture of the ester (30 g.) and 48% hydrobromic acid (150 c.c.) was boiled under reflux for 5 hr.: carbon dioxide evolution from the clear solution had then ceased. The cold solution readily deposited the tetrahydrobromide, which was collected, washed with ethanol, dried, and decomposed with a large excess of saturated aqueous potassium hydroxide. The vigorously stirred sludge was continuously extracted with ether. Distillation of the dried extract gave the highly hygroscopic 1:2-*di*-(1-*piperazinyl*)*ethane* (XIV; R = H), b. p. 166—168·5°/15 mm., m. p. 102° (Found: C, 60·2; H, 11·6; N, 28·0. $C_{10}H_{22}N_4$ requires C, 60·6; H, 11·1; N, 28·3%), readily soluble in cold methanol and ethanol and in hot water, and sparingly so in hot ether, benzene, and light petroleum. For characterisation, 48% hydrobromic acid was cautiously added to a chilled ethanolic solution of the base, the *tetrahydrobromide* rapidly separating; it crystallised as needles, m. p. 270—272° (decomp.) (T.I. 260°), from 95% ethanol (Found: C, 22·75; H, 5·45; N, 10·4. $C_{10}H_{22}N_4,4HBr$ requires C, 23·0; H, 5·0; N, 10·7%). The base gave a *dibenzoyl derivative*, needles, m. p. 136·5—137°, from ethyl acetate (Found: C, 70·5; H, 7·6; N, 13·7%; *M*, in boiling chloroform, 400. $C_{24}H_{30}O_2N_4$ requires C, 70·9; H, 7·4; N, 13·8%; *M*, 406).

This base (11·4 g.) when gently warmed in formic acid (50 c.c.) and 40% aqueous formaldehyde (17 c.c.), underwent vigorous reaction (cooling), after which it was boiled under reflux for 6 hr. The cold solution was diluted with concentrated hydrochloric acid (20 c.c.) and evaporated at 15 mm. The solid residue was basified as before and extracted with ether. Distillation gave 1:2-*di*-(4-*methyl*-1-*piperazinyl*)*ethane* (XIII) (9·9 g., 85%), b. p. 100—103°/0·1 mm., m. p. 38—38·5° (in an open or sealed tube) (Found: C, 63·6; H, 11·3; N, 24·2. $C_{12}H_{26}N_4$ requires C, 63·7; H, 11·5; N, 24·8%). The base is only very slightly volatile in boiling ether, for the ether distillate gave only faint traces of the almost insoluble tetrapicrate described below.

This base was characterised by the following derivatives.

A cold stirred ethanolic solution of the base was cautiously diluted with a slight excess of 48% hydrobromic acid. The precipitated crystalline *tetrahydrobromide*, when recrystallised from 98% ethanol and then dried at 100°/0·5 mm., had m. p. 267° (decomp.) (T.I. 260°) (Found: C, 26·45; H, 5·5; N, 10·0; Br, 58·5. $C_{12}H_{26}N_4,4HBr$ requires C, 26·2; H, 5·45; N, 10·2; Br, 58·15%).

The *tetra*-p-*nitrophenoxide* was precipitated from ethereal solutions as pale lemon crystals, m. p. 182·5—183·5° (decomp.) (T.I. 175°), after crystallisation from ether (Found: C, 55·0; H, 6·3; N, 14·0. $C_{12}H_{26}N_4,4C_6H_5O_3N$ requires C, 55·4; H, 5·9; N, 14·3%). A mixture of this salt and the di-*p*-nitrophenoxide (m. p. 182—183°) of the base (I) had m. p. 166—170°. The two salts differ in that the tetramine salt is more soluble in cold ethanol and ether and is distinct in colour from the deep yellow crystals of the diamine salt.

The *tetra*-2:4-*dinitrophenoxide*, similarly prepared, formed bright yellow crystals, m. p. 221—222° (decomp.) (T.I. 210°) after crystallisation from 95% ethanol (Found: C, 45·2; H, 4·4; N, 17·3. $C_{12}H_{26}N_4,4C_6H_4O_5N_2$ requires C, 44·9; H, 4·4; N, 17·5%).

The addition of the base to picric acid, both in ethanol, precipitated the *tetrapicrate*, golden-yellow needles, m. p. 292° (vigorous decomp.) (T.I. 280°) (from much hot water) (Found: C, 38·2; H, 3·5; N, 19·7. $C_{12}H_{26}N_4,4C_6H_3O_7N_3$ requires C, 37·8; H, 3·35; N, 19·6%). A mixture of this tetrapicrate and the dipicrate (m. p. 290°) of the diamine (I) had m. p. 280° (decomp.) (T.I. 270°); the tetrapicrate is much the less soluble in boiling water, and on melting decomposes much more vigorously.

A methanolic solution of the base was heated with a large excess of methyl bromide at 75° for 12 hr. The products, after evaporation of the unchanged bromide, were taken to dryness in a desiccator at reduced pressure. The powdered residue, when thrice extracted with boiling anhydrous methanol and then recrystallised from 98% methanol, gave the *trimethobromide*, m. p. 285—287° (decomp.) (T.I. 270°) (Found: C, 35·4; H, 6·95; N, 11·0. $C_{15}H_{35}N_4Br_3$ requires C, 35·3; H, 6·85; N, 11·0%).

In an attempt to form the tetramethobromide, an intimate mixture of the base and methyl toluene-*p*-sulphonate (8 mols.) was heated at 130° for 30 min. Unchanged sulphonate was

removed from the gummy product by repeated extraction with ether, but the crystalline residue of quaternary sulphonate proved too deliquescent for useful recrystallisation. Its methanolic solution, when added to a similar solution of lithium bromide, slowly deposited the above trimethobromide, m. p. 290—291° (decomp.) (T.I. 280°) when recrystallised as before (Found : C, 34·85; H, 7·3%).

The m. p. of this trimethobromide is markedly affected by the temperature of immersion and (particularly) by traces of impurity : this applies also to the trimethiodide (p. 1899). The sample of the trimethobromide described below (p. 1896), of m. p. 296° (T.I. 290°), when mixed with triethylenediamine dimethobromide, also of m. p. 296°, had m. p. 287° (decomp.) (T.I. 280°).

The trimethobromide, treated with sodium picrate, both in aqueous solution, deposited the *trimethopicrate*, yellow needles, m. p. 212—212·5° (decomp.) (T.I. 210°) (Found : C, 41·7; H, 4·4; N, 19·2. $C_{33}H_{41}O_{21}N_{13}$ requires C, 41·5; H, 4·3; N, 19·0%).

Thermal Decomposition of 1-2′-*Dimethylaminoethyl*-4-*methylpiperazine Trihydrochloride* (VII).—The pure dry powdered salt was used throughout.

(a) *Under reduced pressure.* These experiments were carried out on a small scale using the apparatus employed for the decomposition of triethylenediamine dimethobromide (see Figure, p. 1890). The pure powdered salt (VII) (1 g.) was heated at 0·004 mm. pressure in a Silicone bath, the temperature of which was slowly raised to 220° and there maintained for 2 hr. A sublimate formed in the tube *A* just above the Silicone surface, but no distillate collected in the receiver. The powdered sublimate, m. p. 259—260° (decomp.) (T.I. 250°), was twice extracted with cold ethanol (2 × 5 c.c.).

The dried residue, consisting of the unchanged (VII), had m. p. 269—270° (decomp.) (T.I. 260°), unaffected by crystallisation from 99% ethanol (Found : C, 38·6; H, 8·8; N, 14·4%) or from ethanol containing 2% of concentrated hydrochloric acid; a mixture with the sample, m. p. 262° (p. 1888), had m. p. 264° (decomp.) (T.I. 260°). It is noteworthy that the ethanolic mother-liquor from the crystallisation of this salt, m. p. 269—270°, when saturated with hydrogen chloride, deposited the salt, m. p. 260° (decomp.) (T.I. 250°). The identity of the salt, m. p. 269—270°, was confirmed by conversion into the trihydrobromide, m. p. 238° (effervescence) (T.I. 230°) (Found : C, 26·3; H, 5·7%), and into the dihydriodide, m. p. 265—266° (T.I. 260°) : the m. p.s of these two salts were unchanged on admixture with authentic samples.

The ethanolic extracts of the sublimate, evaporated in a desiccator, gave residues having m. p. 272—274° and 270—273° (decomp.) (T.I. 260°) respectively. They were united and again extracted with cold ethanol (4 c.c.) leaving a small undissolved portion. The extract, when filtered and evaporated, gave the pure hygroscopic dihydrochloride, m. p. 278° (decomp.) (T.I. 260°), of the amine (VIII) (Found : C, 44·2; H, 9·9; N, 17·5. Calc. for $C_9H_{21}N_3,2HCl$: C, 44·3; H, 9·4; N, 17·2%). This salt, which is markedly more soluble in cold ethanol than the trihydrochloride, was first prepared by Stewart *et al.*[9] by the interaction of 2-chloroethyldimethylamine, 1-methylpiperazine, and sodium carbonate in ethanol; they give m. p. 262—264°.

(b) *At atmospheric pressure.* To ensure uniform heating, a shallow layer of the salt (VII) in only 8 g. lots, contained in a conical flask fitted with a reflux air-condenser, was heated in a Silicone bath for 1 hr. at 280°, and for 30 min. at 250°, *i.e.*, the conditions used by Mann and Mukherjee.[1] The greater part of the small sublimate which formed around the neck of the flask fell back into the main product, which ultimately formed a pale brown liquid. When cold, the solid product was thoroughly chilled, treated with 100% (w/v) aqueous potassium hydroxide and then extracted 8 times with ether. In a typical experiment, the salt (VII) (304 g.) was thus decomposed in batteries of four flasks heated together in a large bath. The united ethereal extracts were dried (KOH), filtered, and distilled, and gave the following main fractions. (i) the ether distillate; (ii) b. p. 128—142°, 43 g.; (iii) b. p. 76—94°/15 mm., 17 g.; (iv) b. p. 75—130°/0·06 mm., 10·3 g. A dark viscous liquid remained.

(i) The ether distillate was extracted with dilute hydrochloric acid, which when evaporated gave a crude hygroscopic hydrochloride (63 g., after thorough drying); repeated recrystallisation of a portion from ethanol eliminated mixed methylamine hydrochlorides and gave 1 : 4-dimethylpiperazine dihydrochloride, m. p. 262° (decomp.) (T.I. 255°) (Found : C, 38·1; H, 8·9%).

Fraction (ii). Refractionation gave 1 : 4-dimethylpiperazine, b. p. 130—133°, identified as its dipicrate, m. p. 295° (vigorous decomp.) (T.I. 285°) (Found : C, 37·9; H, 3·8; N, 19·4%), and its dimethiodide, m. p. 333° (decomp.) (T.I. 325°, sealed tube) (Found : C, 24·2; H, 5·1;

N, 6·7%). When about two-thirds of this fraction had thus passed over the rate of distillation slackened. The residue liquid was cooled and the fractionation restarted under reduced pressure. The remainder of the dimethylpiperazine now distilled at 37—42°/15 mm., but was accompanied by piperazine which sublimed in small quantity in the condenser. These crystals were subsequently collected, drained and identified (*a*) by conversion into the dihydrobromide, m. p. 360° (decomp.) (T.I. 350°), after recrystallisation from 90% ethanol (Found: C, 19·6; H, 5·2%), and (*b*) by sublimation at 0·1 mm., giving the pure base, m. p. and mixed m. p. 106°.

Fraction (iii). Repeated refractionation gave a liquid, b. p. 86—87°/12 mm., apparently a mixture of the base (VIII) and the *base* $C_8H_{19}N_3$ (Found: C, 61·7; H, 12·4%; *M*, cryoscopic in benzene, 169. $C_9H_{21}N_3$ requires C, 63·1; H, 12·4%; *M*, 171. $C_8H_{19}N_3$ requires C, 61·15; H, 12·1%; *M*, 157). The evidence for the former is that the fraction (*a*) in chilled ethanol, when treated with hydrogen chloride, deposited rather sticky crystals, which after three recrystallisations from 98% ethanol afforded the trihydrochloride of the base (VIII), m. p. 262° (effervescence) (T.I. 240°), depressed to 240—243° (decomp.) (T.I. 230°) by admixture with dimethylpiperazine dihydrochloride (Found: C, 38·7; H, 9·05%), and (*b*) gave the chloroplatinate, orange plates, m. p. 242° (decomp.) (T.I. 230°) (Found: C, 13·7; H, 3·0; N, 5·3%), of (VIII). The evidence for the base $C_8H_{19}N_3$ is that the fraction (*a*) with saturated ethanolic oxalic acid gave a *tri(hydrogen oxalate)*, m. p. 215° (effervescence) (T.I. 210°) after crystallisation from aqueous ethanol (Found: C, 39·0; H, 5·85; N, 9·6. $C_8H_{19}N_3,3C_2H_2O_4$ requires C, 39·3; H, 5·9; N, 9·8%) [a mixture of this salt with the similar oxalate, m. p. 228°, of the base (VIII) shrank considerably at 210° and melted at 215—217° (effervescence)], and (*b*) when added in ethanol to dilute nitric acid gave a *trinitrate*, leaflets, m. p. 143° (vigorous decomp.) (T.I. 120°) when crystallised from ethanol–dilute nitric acid (Found: C, 27·8; H, 6·45; N, 24·1. $C_8H_{19}N_3,3HNO_3$ requires C, 27·7; H, 6·4; N, 24·3%) [a mixture with the nitrate, m. p. 164°, of the base (VIII) had m. p. 142—143° (vigorous decomp.) (T.I. 120°)].

The fraction, when treated in methanol with methyl bromide gave the dimethobromide of the base (VIII), m. p. 315° (decomp.) (T.I. 300°) (Found: C, 36·2; H, 7·4%), and with methyl iodide gave the corresponding dimethiodide, m. p. 324° (effervescence) (T.I. 310°) (Found: C, 29·0; H, 5·6; N, 9·4%). The formation of these salts, however, does not differentiate between (VIII) and the base $C_8H_{19}N_3$, for the latter might undergo ready methylation and then quaternisation to give the same products.

The final fraction, b. p. 86—87°/12 mm., always retained an odour resembling that of stale tobacco smoke, whereas the pure synthetic base (VIII) was almost odourless.

Fraction (iv). Repeated fractionation gave two main fractions (*a*), b. p. 77—79°/0·015 g. (4 g.); (*b*) b. p. 105—108°/0·065 mm. (*ca.* 1 g.).

Fraction (*a*), a very faintly green liquid, soluble in water, was almost pure 1:2-di-(4-methyl-1-piperazinyl)ethane (XIII) (Found: C, 64·0; H, 11·4%; *M*, cryoscopic in benzene, 244. Calc. for $C_{12}H_{26}N_4$: C, 63·7; H, 11·5%; *M*, 226). The remainder of the fraction was further purified by conversion into the tetrahydrobromide, hygroscopic plates, m. p. 266° (decomp., gentle effervescence) (T.I. 250°) after four recrystallisations from 98% ethanol and thorough drying (P_2O_5) in a vacuum (Found: C, 26·1; H, 5·4; N, 10·1; Br, 57·8%). This pure salt gave a tetra-*p*-nitrophenoxide, m. p. 183—184° (decomp.) (T.I. 180°) (Found: C, 55·3; H, 5·9; N, 14·4%), a tetra-2:4-dinitrophenoxide, m. p. 220—221° (decomp.) (T.I. 210°) (Found: C, 45·2; H, 4·3; N, 17·75%), and a tetrapicrate, m. p. 292° (vigorous decomp.) (T.I. 280°) (Found: C, 37·8; H, 3·5; N, 19·7%). The base was heated with methanolic methyl bromide at 60° for 6 hr.; the product, worked up as previously described, gave the trimethobromide, m. p. 296° (decomp.) (T.I. 290°) (Found: C, 35·4; H, 6·7%), which in turn gave the trimethopicrate, m. p. 208—210° (decomp.) (T.I. 200°) (Found: C, 41·2; H, 3·8; N, 18·7%). The m. p. of each of these five salts was unaffected by admixture with the corresponding salt prepared from the synthetic tetramine (XIII).

A cold methanolic solution of the amine was diluted with methyl bromide and set aside in a closed flask overnight, crystals rapidly separating. Unchanged bromide was then allowed to evaporate, and the mixture taken to dryness in a desiccator. Recrystallisation of the residue proved unsatisfactory. It was recrystallised from aqueous methanol, giving a crop, m. p. 235—238° (T.I. 200°), too small for reliable investigation: the chilled filtrate was then cautiously treated with 48% hydrobromic acid, giving an immediate crystalline precipitate, m. p. 226—228° (T.I. 200°). It was purified by dissolution in 98% methanol and reprecipitation by the acid;

the *dimethobromide dihydrobromide dihydrate* separated in firm non-hygroscopic crystals, m. p. 240—242° (T.I. 235°) (Found: C, 27·7; H, 6·1; N, 9·1; Br, 52·5. $C_{14}H_{32}N_4Br_2,2HBr,2H_2O$ requires C, 27·4; H, 6·2; N, 9·1; Br, 52·1%). The same compound was obtained when the first methanolic extract of (*a*) the above crude trimethobromide and (*b*) that prepared from the synthetic tetramine (XIII) was similarly treated with hydrobromic acid [Found: (*a*) C, 27·5; H, 6·15; N, 9·15; (*b*) C, 28·0; H, 5·9; N, 9·25%].

An aqueous solution of this salt, when added to one containing sodium picrate and picric acid, deposited the yellow *dimethopicrate dipicrate*, m. p. 232—233° (decomp.) (T.I. 220°) after crystallisation from water and drying at 60°/0·1 mm. for 5 hr. (Found: C, 38·9; H, 3·5; N, 19·0. $C_{26}H_{36}O_{14}N_{10},2C_6H_3O_7N_3$ requires C, 39·0; H, 3·45; N, 19·2%).

The pure tetrahydrobromide, when added to chilled concentrated aqueous potassium hydroxide, liberated the oily base, which rapidly solidified. The mixture was rapidly extracted with ether, and the dried ethereal extract distilled. The tetramine (XIII), b. p. 91°/0·03 mm., readily solidified and the highest m. p. determined was 40—43°; satisfactory analyses were not obtained, possibly owing to the small amounts distilled and consequent slight absorption of water or carbon dioxide (Found: C, 62·8; H, 12·2%; *M*, ebullioscopic in benzene, 218, in ethanol, 230. Calc. for $C_{12}H_{26}N_4$: C, 63·7; H, 11·5%; *M*, 226).

Fraction (*b*), a bright yellow liquid which rapidly became pale olive in colour, and which was almost insoluble in cold water, was apparently 1 : 4-*di*-[2-(4-*methyl*-1-*piperazinyl*)*ethyl*]-*piperazine* (XV) (Found: C, 64·8; H, 11·2%; *M*, cryoscopic in benzene, 325. $C_{18}H_{38}N_6$ requires C, 63·9; H, 11·3%; *M*, 338). A stirred, thoroughly chilled solution of the base in 97% ethanol was cautiously treated dropwise with 48% hydrobromic acid: the crystals which rapidly separated, when then collected, washed with ethanol (in which they were insoluble) and dried, effervesced at *ca.* 100° to a semi-molten mass which again effervesced with darkening and decomposition at 220°. For purification, a solution of the crystals in warm 97% ethanol was allowed to cool to *ca.* 40°, and the hydrobromic acid again cautiously added: the *hexahydrobromide dihydrate* rapidly separated as needles, which effervesced at 96° and again at 240° (darkening and decomp.); these values were unaffected by repetition of this process (Found: C, 25·2; H, 5·3; N, 10·5. $C_{18}H_{38}N_6,6HBr,2H_2O$ requires C, 25·1; H, 5·6; N, 9·8%). This sample was confined over phosphoric anhydride at 0·1 mm. for 14 days, and the presumably anhydrous salt had m. p. 240° (gentle effervescence) (T.I. 130°, 160°) without the preliminary effervescence; on exposure to the air it rapidly became damp, and then in a desiccator reformed the original non-hygroscopic crystalline dihydrate (Found: C, 25·25; H, 5·35%). The salt appeared to be decomposed by hot hydrobromic acid.

This salt gave a *hexapicrate*, which recrystallised from much hot water in flat yellow plates, m. p. 272° (decomp., mild effervescence) (T.I. 240°) (Found: C, 37·8; H, 3·5; N, 20·0. $C_{18}H_{38}N_6,6C_6H_3O_7N_3$ requires C, 37·8; H, 3·3; N, 19·6%). A mixture of this picrate and that of base (VIII) had m. p. 265° (moderate effervescence) (T.I. 240°).

The remainder of the hydrobromide was decomposed with concentrated aqueous potassium hydroxide and extracted in turn with benzene and ether. The united, dried, filtered extracts were evaporated, and the residual oil heated in methanolic methyl bromide at 35—40° for 5 hr. in a sealed tube, heavy sugar-like crystals being deposited. Recrystallisation from 97% methanol gave the non-hygroscopic *trimethobromide dihydrate*, m. p. 305° (decomp., effervescence) (T.I. 300°) (Found: C, 38·6; H, 7·1; N, 12·8. $C_{21}H_{47}N_6Br_3,2H_2O$ requires C, 38·2; H, 7·8; N, 12·75%).

The dark viscous residue obtained in the initial fractionation, when dissolved in benzene, dried, and distilled, gave small indefinite dark fractions which could not be profitably investigated.

Thermal Decomposition of 1-2′-*Dimethylaminoethyl*-4 : 4-*dimethylpiperazinium Chloride Dihydrochloride* (VI).—(A) *Under reduced pressure.* The apparatus used was that shown in the Figure. The powdered salt (VI) (1 g.), when heated at 220°/0·003 mm. for 4 hr., gave a small quantity of a hygroscopic sublimate on the upper, colder portion of the tube *A*, and left a residual friable cream-coloured powder. The receiver *E* contained a very small amount of liquid, which when treated with hydrobromic acid and evaporated gave a negligible residue. The sublimate consisted chiefly of the trihydrochloride (VII), for its aqueous solution when added to aqueous sodium picrate deposited the tripicrate of the base (VIII), m. p. 258—260° (decomp.) (T.I. 250°), after recrystallisation from water (Found: C, 38·3; H, 3·9%); this m. p. was unaffected when this salt was mixed with the authentic tripicrate.

XUM

The residue, m. p. 280° (decomp.) (T.I. 270°), was very soluble in ethanol. Its suspension in boiling acetone, when cautiously diluted with ethanol until clear, and then filtered and cooled, deposited colourless **1-2′-*dimethylaminoethyl*-4 : 4-*dimethylpiperazinium chloride hydrochloride monohydrate***, of unchanged m. p. (Found: C, 43·5; H, 9·8; N, 15·5. $C_{10}H_{24}N_3Cl,HCl,H_2O$ requires C, 43·5; H, 9·85; N, 15·2%). This salt, and also the unrecrystallised residue, when recrystallised from ethanol containing 5% (v/v) of concentrated hydrochloric acid, gave the original dihydrochloride monohydrate (VI) (Found: C, 38·5; H, 9·4; N, 13·5%), m. p. 228° (decomp.) (T.I. 220°), unchanged on admixture with an authentic sample.

(B) ***At atmospheric pressure.*** (1) The salt (VI) (1 g.) was heated in a thin-walled tube in an oil-bath to 235°, and the melt gently stirred until effervescence ceased (*ca.* 5 min.). The cold solid product, when powdered, washed with ethanol, and recrystallised from ethanol containing concentrated hydrochloric acid, gave the trihydrochloride (VII), m. p. 260—261° (decomp.) (T.I. 250°) (Found: C, 58·55; H, 8·4%).

(2) The anhydrous salt (VI) (320 g.) was decomposed in 8 g. lots precisely as the salt (VII), and the product similarly basified and extracted with ether. The united ether extracts on distillation gave the following main fractions: (i) ether distillate; (ii) b. p. 135—144° (25 g.); (iii) b. p. 90—94°/12 mm. (41 g.), with a preliminary very small deposit of crystalline piperazine in the condenser; (iv) b. p. 48—85° (mainly 82—85°)/0·003 mm. (7 g.). The residue (1—2 g.) began to decompose with blackening and without distillation when the temperature of the oil-bath reached 260° (0·0004 mm., internal pressure) and was not further investigated.

The ether distillate (i), treated as previously described, furnished crude 1 : 4-dimethylpiperazine dihydrochloride (31 g.), identified as the pure salt, m. p. 262—263° (decomp.) (T.I. 250°) (Found: C, 38·2; H, 8·9%). Fraction (ii) on refractionation gave 1 : 4-dimethylpiperazine, b. p. 132—134°, identified as its dipicrate, m. p. 293° (vigorous decomp.) (T.I. 280°) (Found: C, 37·8; H, 3·0; N, 19·5%), and its dimethiodide, m. p. 330° (decomp.) (T.I. 320°, sealed tube) (Found: C, 24·2; H, 5·1; N, 6·9%). Fraction (iii) on refractionation gave a liquid, b. p. 91—92·5°/12 mm., consisting of the almost pure base (VIII) (Found: C, 62·5; H, 11·85%; *M*, cryoscopic in benzene, 169). In chilled ethanolic solution, when treated with hydrogen chloride, it gave a copious deposit of the trihydrochloride (VII), m. p. 262° (decomp.) (T.I. 250°) after crystallisation from 98% ethanol (Found: C, 38·6; H, 8·2%). It also gave the trinitrate, m. p. 154° (vigorous decomp.) (T.I. 140°) unchanged by repeated recrystallisation (Found: C, 30·4; H, 6·9; N, 23·6%), the chloroplatinate, orange crystals, m. p. 242° (decomp.) (T.I. 235°) (Found: C, 13·5; H, 3·0; Pt, 37·0%), the picrate, yellow crystals, m. p. 252° (decomp.) (T.I. 240°), and the dimethiodide dimethanolate, 318° (decomp.) (T.I. 300°) (Found: C, 29·6; H, 5·8; N, 9·1%). The identity of these salts was confirmed by mixed m. p. determinations. A sample of the crude fraction (iii) when set aside for several months deposited a trace of crystalline piperazine.

Fraction (iv) on refractionation gave almost pure tetramine (XIII), b. p. 88—90°/0·002 mm. (Found: C, 62·9; H, 10·6%; *M*, cryoscopic in benzene, 240). This sample gave the hygroscopic tetrahydrobromide, m. p. 266° (effervescence) (T.I. 260°) after crystallisation from ethanol (Found: C, 25·9; H, 5·9; N, 9·9%), and the *tetra(hydrogen oxalate)*, prepared in ethanol and recrystallised from aqueous ethanol, m. p. 239° (effervescence) (T.I. 230°) (Found: C. 40·7; H, 5·8; N, 9·3. $C_{12}H_{26}N_4,4C_2H_2O_4$ requires C, 40·9; H, 5·85; N, 9·55%).

Derivatives of the tetramine (XIII). These additional derivatives were prepared from the pure base for comparison with those of other amines (see Table). Ethanolic solutions of the base and of hydrogen chloride were mixed and evaporated to dryness in a desiccator, giving fine, non-hygroscopic crystals, m. p. 286—288° (decomp.) (T.I. 280°), of the *tetrahydrochloride dihydrate* (Found: C, 35·8; H, 7·6. $C_{12}H_{26}N_4,4HCl,2H_2O$ requires C, 35·3; H, 8·4%). A cold ethanolic solution of this salt, treated with hydrogen chloride, deposited fine crystals of unchanged m. p., which when heated at 60°/0·1 mm. for 7 hr., furnished the anhydrous *salt* (Found: Cl^-, 38·4. $C_{12}H_{26}N_4,4HCl$ requires Cl, 38·1%). This salt is thus markedly different from the deliquescent dihydrochloride of the base (I).

An ethanolic solution of the base, when treated dropwise with concentrated hydriodic acid, deposited crystals, which after crystallisation from 98% ethanol, afforded the ***trihydriodide monohydrate***, m. p. 231° (decomp.) (T.I. 220°) (Found: C, 23·3; H, 4·6; N, 8·5. $C_{12}H_{26}N_4,3HI,H_2O$ requires C, 23·0; H, 4·9; N, 8·9%). The crystals on exposure to light slowly develop a buff colour.

A cold methanolic solution of the base, with an excess of methyl iodide, readily deposited

crystals which were collected after 2 hr. and recrystallised from 95% methanol, furnishing the *dimethiodide hemihydrate*, m. p. 288° (T.I. 275°) (Found : C, 32·4; H, 6·4. $C_{14}H_{32}N_4I_2,0{\cdot}5H_2O$ requires C, 32·4; H, 6·4%), which heated at 50°/0·1 mm. for 5 hr., gave the anhydrous *salt* (Found : C, 32·9; H, 6·4; N, 10·8. $C_{14}H_{32}N_4I_2$ requires C, 32·9; H, 6·3; N, 11·0%). When the initial solution was set aside overnight, the crystals became contaminated with the trimethiodide.

The above solution, when boiled under reflux for 4 hr., deposited crystals which, recrystallised from 95% methanol, gave the *trimethiodide*, m. p. 270° (T.I. 260°) (Found : C, 27·7; H, 5·2; N, 8·3. $C_{13}H_{35}N_4I_3$ requires C, 27·6; H, 5·4; N, 8·6%). Repetition of this experiment, but with the solution heated in a sealed tube at 75° for 5 hr., gave the same salt, m. p. 266° (T.I. 260°) (Found : N, 8·6%). In case a tetramethiodide was formed in these experiments and decomposed to the trimethiodide when heated during recrystallisation, the above solution was heated in a sealed tube at 80° for 5 hr., and the excess of methyl iodide then allowed to evaporate at room temperature from the mixture. The crystals were collected, washed with methanolic methyl iodide, and dried in a vacuum (P_2O_5) for 3 days to ensure absence of a hydrate. The residue was crude trimethiodide (Found : C, 27·2; H, 5·3; N, 8·2%) but having m. p. 248—249° (decomp.) (T.I. 240°), increased to 274—276° (decomp.) (T.I. 260°) on crystallisation from methanol.

It is noteworthy that the trimethobromide and the above di- and tri-methiodide are insoluble in boiling anhydrous methanol, but readily dissolve on the addition of a very small amount of water.

An aqueous solution of the trimethiodide, when added to an aqueous solution of sodium picrate and picric acid, gave yellow crystals which, after recrystallisation from water, furnished the trimethopicrate, m. p. 209—210° (decomp.) (T.I. 200°) (Found : C, 41·7; H, 4·2%) : in these circumstances a trimethopicrate picrate is either not formed or dissociates during crystallisation to the trimethopicrate.

The addition of 50% nitric acid to a cold ethanolic solution of the base deposited the *tetranitrate* as a gel which did not crystallise for 2 days and was collected with difficulty. Recrystallisation from aqueous ethanol readily gave large glistening plates, m. p. 245° (effervescence) (T.I. 228°) (Found : C, 30·0; H, 6·1. $C_{12}H_{26}N_4,4HNO_3$ requires C, 30·1; H, 6·3%). If immersed at 230° or above, it immediately explodes.

Dilute solutions of the base and of chloroplatinic acid, both in dilute hydrochloric acid, when mixed deposited the *di(chloroplatinate)*, orange plates, m. p. 287° (decomp.) (T.I. 270°), unchanged by crystallisation from water (Found : C, 14·0; H, 3·2; N, 5·55; Pt, 37·2. $C_{12}H_{26}N_4,2H_2PtCl_6$ requires C, 13·8; H, 2·9; N, 5·4; Pt, 37·3%). A mixture of this salt and the chloroplatinate of dimethylpiperazine (m. p. 282°) had m. p. 273° (decomp.) (T.I. 260°).

We are greatly indebted to Mr. H. R. Watson for the preparation of the amine (XIII) and several derivatives, to Dr. A. Senior for molecular-weight determinations, and to Imperial Chemical (Pharmaceuticals) Ltd. and Mr. O. D. Standen for the therapeutic tests.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, November 14th*, 1956.]

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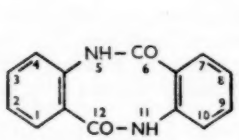
356. *The Beckmann Rearrangement of the Dioximes of Anthraquinone and* 1 : 5-*Dichloroanthraquinone.*

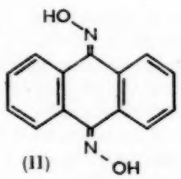
By H. N. Rydon, N. H. P. Smith, and D. Williams.

The Beckmann rearrangement of anthraquinone dioxime with polyphosphoric acid gives dianthranilide (I), in good yield; the dioxime therefore has the *anti*-configuration. 1 : 5-Dichloroanthraquinone yields a mixture of two dioximes which are shown, on the basis of the products they give on Beckmann rearrangement, to be the *trans-trans*- and *cis-trans*-compounds. Both oximes are cyclised by alkali, at approximately equal rates, to the bis*iso*-oxazole (VII), and it is shown that this cyclisation is accompanied by stereochemical inversion; the general validity of such cyclisations for the assignment of oxime configurations is questioned.

Dianthranilide * (I), a nitrogen analogue of disalicylide, the parent of a series extensively investigated by Baker and his colleagues,[1] was prepared, in poor yield, by Schroeter and Eisleb [2] by a five-stage process from anthranilic acid. A much simpler route appeared to be by the Beckmann rearrangement of anthraquinone *anti*-dioxime (II). A dioxime of anthraquinone, of unknown stereochemical configuration, was prepared by Meisenheimer and Mahler [3] by the pyridine method, but there is no record of its having been subjected to the Beckmann rearrangement. Beckmann and Liesche [4] carried out such a



(I)



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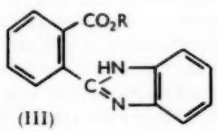


(III)

rearrangement with anthraquinone monoxime and obtained a keto-lactam, the oxime of which, on further Beckmann rearrangement, afforded 2-*o*-carboxyphenylbenziminazole (III ; R = H), no doubt by way of *NN'*-phthaloyl-*o*-phenylenediamine.

In view of the failure of Beckmann and Liesche [4] to bring about the Beckmann rearrangement of benzoquinone dioxime with the usual reagents, we subjected anthraquinone dioxime to the action of hot polyphosphoric acid, which has been shown [5] to be remarkably effective for the rearrangement of ketoximes. The product, obtained in good yield, was shown to be dianthranilide (I) by comparison with a specimen prepared by the method of Schroeter and Eisleb; [2] no trace of the benziminazole (III; R = H) or of the derived tetracyclic lactam (*iso*indolobenziminazole) could be found in the reaction product. This result establishes the *anti*-configuration (II) for the anthraquinone dioxime obtained by the pyridine procedure.[3]

We next turned our attention to the dioximes of 1 : 5-dichloroanthraquinone. Three

* The Ring Index names for (I) (No. 2093) are phenhomazine-6 : 12-dione or, more systematically, dibenzo[*b*, *f*][1, 5]diazocine-6 : 12-dione, but we prefer dianthranilide as being both more intelligible and more euphonious; we have adopted the Ring Index numbering.

[1] Baker, McOmie, and Ollis, *J.*, 1951, 200; Baker, Ollis, and Zealley, *ibid.*, p. 201; Baker, Gilbert, Ollis, and Zealley, *ibid.*, p. 209; Baker, Gilbert, and Ollis, *J.*, 1952, **1443**; Baker, El-Nawawy, and Ollis, *ibid.*, p. 3163; Baker, Harborne, Price, and Rutt, *J.*, 1954, 2042.

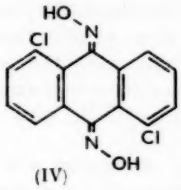
[2] Schroeter and Eisleb, *Annalen*, 1909, **367**, 101.

[3] Meisenheimer and Mahler, *ibid.*, 1934, **508**, 191.

[4] Beckmann and Liesche, *Ber.*, 1923, **56**, 1.

[5] Horning and Stromberg, *J. Amer. Chem. Soc.*, 1952, **74**, 2680; Horning, Stromberg, and Lloyd, *ibid.*, p. 5153.

stereoisomerides are possible; two of these are *anti*-forms, which we designate * as *cis-cis*- (IV), and *trans-trans*- (V), the third, *syn*, form being the *cis-trans*-compound, (VI):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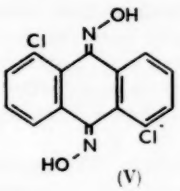
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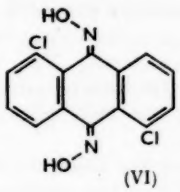
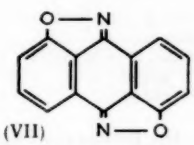
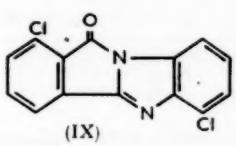
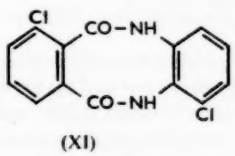

(VI)

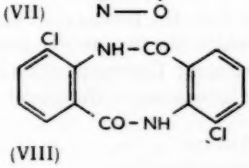
1 : 5-Dichloroanthraquinone forms a dioxime more readily than does anthraquinone, and Freund and Achenbach [6] subjected a mixture of dioximes obtained by the action of hydroxylamine on 1 : 5-dichloroanthraquinone to the action of hot alkali, obtaining the bis*iso*oxazole (VII), and a dioxime, m. p. 245°, which they found to be unaffected by alkali and to which they accordingly ascribed the *trans-trans*-configuration (V); the bis*iso*-oxazole was regarded as having been formed from the *cis-cis*-dioxime (IV), which was, however, not isolated.

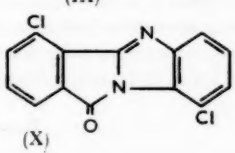
Repetition of Freund and Achenbach's work with the mixture of 1 : 5-dichloroanthraquinine dioximes obtained by the pyridine procedure gave the bis*iso*oxazole (VII) and a dioxime, m. p. 262°; the latter was, however, not the pure *trans-trans*-compound since Beckmann rearrangement gave two products [(VIII) and (IX) or (X), the former prepon-


(VII)


(IX)


(XI)


(VIII)


(X)

derating]. The original mixture of dioximes with acetyl chloride in pyridine [7] gave a mixture of diacetyl derivatives which was readily separated into its components by treatment with cold acetic anhydride.

The diacetyl derivative insoluble in acetic anhydride, on hydrolysis with sodium hydroxide in dioxan, yielded a dioxime, m. p. 250°. Beckmann rearrangement of this with polyphosphoric acid gave a dichlorodianthranilide, which yielded dianthranilide (I) on catalytic hydrogenolysis and was shown to be 4 : 10-dichlorodianthranilide (VIII), by hydrolysis to 3-chloroanthranilic acid [8] ($CO_2H = 1$). On the basis of a Beckmann *trans*-rearrangement we assign the *trans-trans*-configuration (V) to this dioxime.

Similar hydrolysis of the diacetyl derivative soluble in acetic anhydride yielded another dioxime, m. p. 267°. Beckmann rearrangement of this yielded a dichloro-oxo-*iso*indolobenziminazole (IX) or (X); this structure is confirmed by the close similarity of the light

* We use the terms *syn* and *anti* to describe the mutual stereochemical relations of the oxime groups, and *cis* and *trans* to describe the configurations of these groups with respect to the nearer chlorine atom.

[6] Freund and Achenbach, *Ber.*, 1910, **43**, 3251.
[7] Cf. Einhorn and Hollandt, *Annalen*, 1898, **301**, 95.
[8] Baker, Schaub, Joseph, McEvoy, and Williams, *J. Org. Chem.*, 1952, **17**, 143.

absorption to that of the chlorine-free compound [9,10] and also by the similarity of the light absorption of the derived 2-(chloro-methoxycarbonylphenyl)chlorobenziminazole to that of the chlorine-free analogue, 2-*o*-methoxycarbonylphenylbenziminazole [9] (III; R = Me); we have no evidence to enable us to distinguish between structures (IX) and (X). The formation of an *iso*indolobenziminazole from the dioxime of m. p. 267° shows this to be the *cis-trans*-compound (VI), without any assumption concerning the stereochemical course of the Beckmann rearrangement, since either *cis*- or *trans*-rearrangement would yield initially the chlorophthaloyl-chloro-*o*-phenylenediamine (XI), which could yield either (IX) or (X).

No trace of the third, *cis-cis*-dioxime (IV) postulated by Freund and Achenbach [6] could be found in the crude mixture of 1 : 5-dichloroanthraquinone dioximes; neither could its expected rearrangement product, 1 : 7-dichloroanthraquinone, be found in the Beckmann rearrangement product from this mixture. The absence of this stereoisomeride is not surprising, since models show considerable overlapping of the chlorine atoms and the hydroxyimino-group.

Contrary to expectation, and to the statement of Freund and Achenbach,[6] both 1 : 5-dichloroanthraquinone dioximes give the bis*iso*oxazole (VII) when heated with dilute alkali. Although qualitative observations of the rate of formation of (VII) supported the configurations assigned to the two diacetyl derivatives it seemed desirable to confirm these by direct measurement of the rates of cyclisation of the two oximes. In one series of experiments this was done by weighing the *iso*oxazole formed in 2N-sodium hydroxide at 100°; in a second, the liberation of chloride ion in 0·5N-potassium hydroxide at 100° was measured; the results, expressed as first-order velocity constants, were as follows:

	k_1 (hr.$^{-1}$)	
Oxime	Bis*iso*oxazole formation in 2N-NaOH	Cl^- liberated in 0·5N-KOH
trans-trans (V)	0·184	0·136
cis-trans (VI)	0·173	0·152

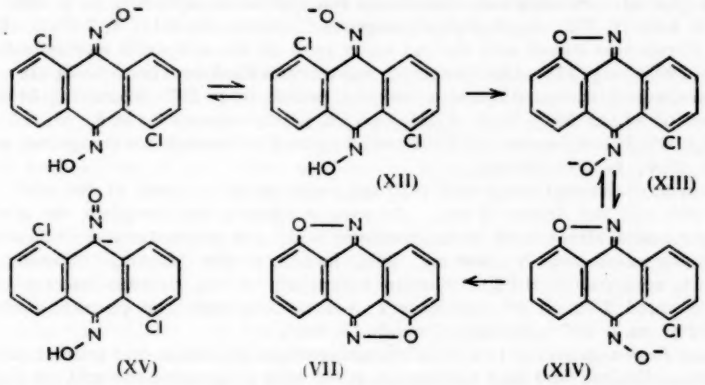
The small difference in the rate of formation of the bis*iso*oxazole from the two oximes was very surprising and an experiment was therefore carried out in which the two pure oximes were each heated at 100° with 0·5N-potassium hydroxide for three hours; the composition of the recovered oxime was ascertained by acetylation, followed by separation of the diacetyl derivatives. The results were:

		Recovered oxime Composition (%)	
Starting material	Yield (%)	(V)	(VI)
trans-trans (V)	69	35	65
cis-trans (VI)	56	23	77

Clearly, bis*iso*oxazole formation is preceded, or accompanied, by stereochemical interconversion of the two oximes with production of an equilibrium mixture. It is probable that only one hydroxyimino-group is ionised under the reaction conditions and the relative insensitivity of the reaction rate to hydroxyl-ion concentration supports the view that the cyclisation involves the oximate anion, rather that the un-ionised hydroxyimino-group. The probable reaction sequence is as annexed, in which the slowest, rate-determining stage must be the first cyclisation, (XII) ⟶ (XIII); this is necessitated by the overall first-order kinetics of the reaction and the absence of the mono*iso*oxazole [as (XIII) or (XIV)] from the products of the interrupted hydrolyses. The second cyclisation might well be expected to be faster than the first, since the closure of the first *iso*oxazole ring renders the whole tetracyclic system rigidly planar; the inverted anion (XIV) is thus fixed in a position peculiarly favourable to further cyclisation to the bis*iso*oxazole (VII). It seems probable that the stereochemical inversions proceed by way of the nitroso-carbanions, *e.g.*, (XV).

[9] Bistrzycki and Lecco, *Helv. Chim. Acta*, 1921, **4**, 425.
[10] Porai-Koshitz and Antoshulskaya, *J. Gen. Chem.* (*U.S.S.R.*), 1943, **13**, 339.

The stereochemical inversion of oximes under the influence of alkali was observed by early workers,[11] but its significance for the classical work of Meisenheimer [12] on the cyclisation of the oximes of *o*-substituted aromatic ketones has not been generally appreciated. In one of Meisenheimer's papers [13] stereochemical inversion under the influence



of alkali was observed to accompany *iso*oxazole ring formation; in this case, the rates of the two reactions were sufficiently different to justify Meisenheimer in neglecting the stereochemical inversion when interpreting his results. In our case, however, it is clearly not possible to ignore the stereochemical inversion and it therefore appears that it is not generally safe to assign oxime configurations on the basis of cyclisations carried out in alkali; ketoxime configurations are thus more safely based on the Beckmann rearrangement, the *trans*-nature of which is now overwhelmingly supported by other evidence.[12]

Experimental

Figures for light absorption are $\lambda_{max.}$ in mμ, followed by $\varepsilon_{max.}$ in parentheses.

Beckmann Rearrangement of Anthraquinone Dioxime.—Anthraquinone dioxime [3] (2 g.) was stirred into polyphosphoric acid [14] (60 g.) at 100° and the mixture heated, with stirring, in an oil-bath at 140° for 80 min.; dissolution was complete in 60 min. The product was poured into water (300 ml.); recrystallisation of the precipitated solid from water yielded dianthranilide (I) (1·7 g., 85%), m. p. 334° (Found: C, 70·45; H, 4·5; N, 11·7. Calc. for $C_{14}H_{10}O_2N_2$: C, 70·6; H, 4·2; N, 11·75%); the m. p. was not depressed on admixture with a specimen of dianthranilide, m. p. 330°, prepared by Schroeter and Eisleb's method.[2]

1 : 5-*Dichloroanthraquinone Dioximes.*—1 : 5-Dichloroanthraquinone (12 g.) and hydroxylamine hydrochloride (72 g.) were refluxed in pyridine (400 ml.) for 36 hr. The cooled solution was stirred into an excess of 2N-sulphuric acid and ice, and the precipitated solid digested with cold 2N-sodium hydroxide (150 ml.). After filtration from unchanged quinone, the filtrate was acidified and the precipitate (15 g.) dried at 50° and exhaustively extracted with boiling chlorobenzene. The insoluble mixture of dioximes (5·25 g., 40%), washed with light petroleum (b. p. 60—80°) and dried at 50°, had m. p. 225° (decomp.) (Found: N, 9·00%).

Such a mixture of dioximes (12 g.) was refluxed for 7 hr. with 2N-sodium hydroxide. The insoluble bis*iso*oxazole (VII) (5·1 g., 56%), recrystallised from acetic acid, had m. p. 330—335° (decomp.) (Found: N, 12·1. Calc. for $C_{14}H_8O_2N_2$: N, 12·0%). Acidification of the filtrate gave a mixture of dioximes (4·0 g., 33%), m. p. 262° (decomp.).

Another sample of the original mixture of dioximes (6·5 g.), in anhydrous pyridine (50 ml.),

[11] For refs. see Meisenheimer and Theilacker in K. Freudenberg, "Stereochemie," Leipzig, 1933, p. 1030; cf. Montgomery and Dougherty, *J. Org. Chem.*, 1952, **17**, 823.
[12] For references see Blatt, *Chem. Rev.*, 1933, **12**, 220.
[13] Meisenheimer, Zimmermann, and Kummer, *Annalen*, 1926, **446**, 205.
[14] Bell, *Ind. Eng. Chem.*, 1948, **40**, 1464.

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was treated with acetyl chloride (3·5 g.). After 24 hr. at room temperature, the mixture was poured into ice and 2N-sulphuric acid. The precipitated solid was washed with 2N-sulphuric acid and water and dried in a vacuum-desiccator. This mixture of diacetyl derivatives (8·3 g.) was stirred at room temperature for 3½ hr. with redistilled acetic anhydride (50 ml.). The insoluble material (5·1 g., 62%), m. p. 210—215° (decomp.), was recrystallised from dioxan, affording 1 : 5-*dichloroanthraquinone* trans-trans-*diacetyldioxime* as leaflets, m. p. 236° (Found : C, 55·5; H, 3·0; N, 7·2. $C_{18}H_{12}O_4N_2Cl_2$ requires C, 55·25; H, 3·1; N, 7·2%). The acetic anhydride filtrate was stirred with ice and water until all the anhydride was hydrolysed; the solid (2·5 g., 30%), m. p. 175—185° (decomp.), was recrystallised from benzene–hexane, affording the *cis-trans*-diacetyldioxime as a *benzene complex*, prisms, m. p. 207° (Found : C, 58·9; H, 3·4; N, 6·5; loss of wt. at 100°, 10·4. $C_{18}H_{12}O_4N_2Cl_2,\frac{1}{2}C_6H_6$ requires C, 58·6; H, 3·5; N, 6·5; C_6H_6, 9·1%), which lost benzene at 50°/1 mm. to give the benzene-free compound, m. p. 207° (Found : C, 55·6; H, 3·1; N, 7·4%).

The *trans-trans*-diacetyl compound (650 mg.) was gently warmed at 50° with N-sodium hydroxide (6·7 ml.) and dioxan (1 ml.). As soon as solution was complete, the mixture was cooled in ice and acidified with 2N-hydrochloric acid; the precipitated 1 : 5-*dichloroanthraquinone* trans-trans-*dioxime* (V) (500 mg., 98%) had m. p. 250° (decomp.) (Found : N, 9·45. $C_{14}H_8O_2N_2Cl_2$ requires N, 9·1%). Similar hydrolysis of the *cis-trans*-diacetyl compound (650 mg.) required 3 hr. at 60° and gave 1 : 5-*dichloroanthraquinone* cis-trans-*dioxime* (VI), (470 mg., 92%), m. p. 267° (decomp.) (Found : N, 9·0%).

Beckmann Rearrangement of 1 : 5-*Dichloroanthraquinone Dioximes*.—(a) trans-trans-*Dioxime*. The *trans-trans*-dioxime (400 mg.) was heated at 90° with polyphosphoric acid (12 g.) for 2 hr. The clear pale yellow solution was cooled and poured into ice-water (50 ml.), and the precipitated solid recrystallised from aqueous 2-ethoxyethanol, affording 4 : 10-*dichlorodianthranilide* (VIII) (290 mg., 72%), as plates, m. p. 307° (Found : C, 55·0; H, 2·7; N, 8·8. $C_{14}H_8O_2N_2Cl_2$ requires C, 54·8; H, 2·6; N, 9·1%).

This product (200 mg.) was hydrogenated in ethanol (40 ml.), containing potassium hydroxide (1 g.), over 2% palladised calcium carbonate (1 g.). When hydrogen uptake ceased the mixture was filtered, neutralised (10N-hydrochloric acid), and evaporated under reduced pressure. Recrystallisation of the residue from water gave dianthranilide (145 mg., 93%), m. p. and mixed m. p. 336°.

Another sample (100 mg.) was refluxed for 24 hr. with 20% aqueous potassium hydroxide (5 ml.). Acidification and recrystallisation from water gave 3-chloroanthranilic acid (90 mg., 81%), needles, m. p. 194°, not depressed on admixture with a specimen, m. p. 194°, prepared by the method of Baker *et al.*[8] who give m. p. 188°.

(b) cis-trans-*Dioxime*. The *cis-trans*-dioxime (700 mg.) was similarly rearranged with polyphosphoric acid (20 g.). Recrystallisation of the product from 2-ethoxyethanol gave 1 : 6(or 4 : 9)-*dichloro*-11-*oxo*iso*indolo*[2 : 1-*a*]*benziminazole* (Ring Index No. 2271) (IX or X) (380 mg., 58%) as yellow needles, m. p. 282° (Found : C, 58·8; H, 2·0; N, 9·8; Cl, 24·8. $C_{14}H_6ON_2Cl_2$ requires C, 58·2; H, 2·1; N, 9·7; Cl, 24·5%); light absorption in ether : 238 (28,000), 274 (35,800), 310 (5,400), 313 (7,800), 355 (7,800). An authentic specimen of 11-oxo-*iso*indolo[2 : 1-*a*]benziminazole[9,10] showed the following light absorption in ether : 235 (22,600), 271 (35,400), 290 (8,400), 300 (10,000), 335 (4,900).

The dichloro-oxo*iso*indolobenziminazole (500 mg.) was suspended in methanol (5 ml.) and treated with 2N-sodium hydroxide (1 drop). After 10 min. at room temperature, a homogeneous colourless solution was obtained, from which water precipitated 4(or 7)-*chloro*-2-[3(or 6)-*chloro*-2-*methoxycarbonylphenyl*]*benziminazole* (510 mg., 92%), which crystallised from aqueous methanol in plates, m. p. 191—192° (Found : N, 8·6. $C_{15}H_{10}O_2N_2Cl_2$ requires N, 8·7%); light absorption in ether : 242·5 (13,800), 305 (19,400); when heated above its m. p. the compound resolidifies to give the parent compound (IX or X), m. p. 282°. Authentic 2-*o*-methoxycarbonylphenylbenziminazole[9] (III; R = Me) showed the following light absorption in ether : 237·5 (11,600), 303 (13,500).

Similar treatment of the dichloro-compound with 2-ethoxyethanol and alkali gave 4(or 7)-*chloro*-2-[3(or 6)-*chloro*-2-2′-*ethoxyethoxycarbonylphenyl*]*benziminazole* (73% yield), which crystallised from aqueous 2-ethoxyethanol in plates, m. p. 175° (Found : C, 57·7; H, 4·3; N, 7·3. $C_{18}H_{16}O_3N_2Cl_2$ requires C, 57·0; H, 4·2; N, 7·4%).

(c) *Mixed dioximes*. Rearrangement of the original mixture of stereoisomeric dioximes (4 g.) with polyphosphoric acid (120 g.) at 150° gave a product (3·4 g.) which was recrystallised

from 2-ethoxyethanol. Recrystallisation of the first crop from ethanol and again from 2-ethoxyethanol gave the dichloro-oxo*iso*indolobenziminazole, (IX or X) (0·6 g., 15%), m. p. 284°. Addition of water to the original 2-ethoxyethanol mother-liquors and recrystallisation of the precipitate from ethanol–ether gave 4 : 10-dichlorodianthranilide (VIII) (2·1 g., 52%), m. p. 292°.

Similar treatment of the mixed dioximes remaining after refluxing the original mixture with alkali (p. 1903) likewise gave the benziminazole derivative (18%) and 4 : 10-dichlorodiathranilide (40%).

Action of Alkali on the 1 : 5-*Dichloroanthraquinone Dioximes.*—(a) *Qualitative experiments.* (i) The *trans-trans*-diacetyldioxime (100 mg.) was refluxed for 22 hr. with 2N-sodium hydroxide (2 ml.) and water (5 ml.). Dissolution was complete when the temperature reached 80° and the bis*iso*oxazole began to separate after 30 min. The insoluble product (60 mg., 100%), recrystallised from 2-ethoxyethanol, gave the bis*iso*oxazole (VII) as golden-yellow needles, m. p. 328° (decomp.) (Found : N, 12·1. Calc. for $C_{14}H_6O_2N_2$: N, 12·0%) (Freund and Achenbach [6] give m. p. 304°).

(ii) The *cis-trans*-diacetyldioxime (300 mg.) was similarly treated with 2N-sodium hydroxide (4 ml.) and water (10 ml.). Dissolution occurred at a lower temperature and bis*iso*oxazole began to separate almost at once. The insoluble product (180 mg., 100%) crystallised from 2-ethoxyethanol in golden-yellow needles, m. p. and mixed m. p. 327—328° (decomp.).

(b) *Kinetic experiments.* (i) The stereoisomeric dioximes (1 g.) were refluxed, with mechanical stirring, with 2N-sodium hydroxide. At intervals, the reaction mixture was cooled in ice, the precipitated bis*iso*oxazole filtered off and washed with a little water, and the filtrate returned to the reaction vessel for continued heating; the precipitates were further washed with water, dried, and weighed. In spite of the obvious experimental inadequacies the log plots were satisfactorily linear for 5 hr. (*ca.* 60% reaction) and led to the following first-order velocity constants : *trans-trans*-dioxime, 0·184 hr.$^{-1}$; *cis-trans*-dioxime, 0·173 hr.$^{-1}$.

(ii) The dioximes (153·5 mg.) were dissolved in N-potassium hydroxide (5 ml.), and the solutions made up to 10 ml. with water. Portions (1 ml.) were sealed in separate tubes and heated at 100° in a steam-bath. At intervals, tubes were withdrawn, cooled in ice, and opened; chloride ion was then determined by Volhard's method after acidification with nitric acid. The log plots were again satisfactorily linear for 5 hr. and led to the following first-order velocity constants : *trans-trans*-dioxime, 0·136 hr.$^{-1}$; *cis-trans*-dioxime, 0·152 hr.$^{-1}$.

(c) *Interrupted hydrolyses.* (i) The *trans-trans*-dioxime (1·52 g.) was heated for 3 hr. with 0·5N-potassium hydroxide (99 ml.). The insoluble bis*iso*oxazole (0·225 g., 19·4%) had m. p. 319° (decomp.), raised to 327—328° (decomp.) by recrystallisation from 2-ethoxyethanol. The aqueous filtrate was acidified and the precipitated solid (1·21 g., 80%) filtered off, washed, and dried in a vacuum-desiccator. This mixture of dioximes was acetylated, in the usual manner, with acetyl chloride (0·63 g.) in pyridine (10 ml.). The crude product (1·51 g.) was kept in acetic anhydride (12 ml.), with occasional shaking, for 24 hr. at room temperature. The insoluble *trans-trans*-diacetyldioxime (0·469 g., 24·3%) had m. p. and mixed m. p. 232—233° (decomp.) after recrystallisation from acetic anhydride; the soluble *cis-trans*-diacetyldioxime (0·891 g., 46·1%), precipitated by water in the usual manner, had m. p. and mixed m. p. 204—206° after recrystallisation from benzene–hexane.

(ii) The *cis-trans*-dioxime (1·54 g.), treated in the same way, yielded : (i) bis*iso*oxazole (0·366 g., 31·0%), m. p. 324—326° (decomp.) after recrystallisation from 2-ethoxyethanol; (ii) *trans-trans*-diacetyldioxime (0·324 g., 12·6%), m. p. and mixed m. p. 234—235° (decomp.) after recrystallisation from aqueous dioxan; (iii) *cis-trans*-diacetyldioxime (0·857 g., 43·7%), m. p. and mixed m. p. 197—201° after recrystallisation from benzene–hexane.

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MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY,
MANCHESTER, 1.

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357. *Kinetic Form of the Benzidine and Semidine Rearrangements.*

By C. A. Bunton, C. K. Ingold, and M. M. Mhala.

The rate of rearrangement of hydrazobenzene to benzidine and diphenyline in the presence of perchloric acid in 60% aqueous dioxan is correlated with Hammett acidity functions rather than with acid concentration, the dependence being quadratic at low acidities. The rearrangement thus takes place in a second conjugate acid, formed wholly by specific hydrogen-ion catalysis, *i.e.*, by two successive pre-equilibria which desolvate the two successively adding protons. This conclusion is confirmed by the unprecedentedly large acceleration which is observed when the water in the solvent is replaced by deuterium oxide. The rearrangement of 4 : 4′-dimethylhydrazobenzene to the *o*-semidine shows a similar quadratic dependence on acid; that is, the benzidine and semidine rearrangements have an identical kinetic form. These results delimit permissible theories of the mechanism of the benzidine and semidine rearrangements.

The considerable body of previous work on the kinetics of benzidine rearrangements still leaves several points in a more or less uncertain state. We try here to settle some of these, in order to clear the ground for a new attack on the mechanism of these rearrangements.

(1) *Kinetic Dependence of the Benzidine Rearrangement on Acidity*

The first point relates to the form of the dependence on acid of the rate of this rearrangement under catalysis by a strong acid. Van Loon [1] originally recorded data in approximate agreement with the conclusion that the rate of rearrangement of hydrazobenzene, under catalysis by hydrochloric acid, is proportional to the square of the concentration of the acid. More recently, Hammond and Shine [2] reached this conclusion, on the basis of measurements in 75% aqueous ethanol, at what was described as constant ionic strength, sodium perchlorate being added to the hydrogen chloride to make up a constant total-electrolyte concentration of 0·4M. Carlin, Nelb, and Odioso,[3] working in 95% aqueous ethanol with lithium chloride to make up the " ionic strength ", obtained generally confirmatory results, and showed in addition that the product ratio, benzidine : diphenyline, is independent of the acid concentration. For the rearrangement of *o*-hydrazotoluene in similar conditions, Carlin and Odioso [4] observed a kinetic order of 1·6 in acid, whereas for that of *m*-hydrazotoluene the order was close to 2·0. For the rearrangement of hydrazobenzene in 90% aqueous ethanol, but in otherwise similar conditions, Croce and Gettler [5] obtained results indicating an order of about 1·85 in acid.

Concerning the main exception to an otherwise fair agreement, Carlin and Odioso point out [4] that, if rearrangement is assumed always to take place through the second conjugate acid of the hydrazo-compound, a lower-than-second order in the catalytic acid could be understood on the basis that during reaction the storage of hydrazo-compound as its first conjugate acid is considerable : obviously if it were total, the order in acid could drop to unity. The greater basicity of *o*-hydrazotoluene than of the other hydrazobenzenes could thus be the cause of the observed low kinetic order in this case.

It may, however, be questioned whether the kinetic dependence of these rearrangements on acidity should be referred to hydrogen-ion concentration. Water is not stoicheiometrically involved and it is thus possible that the relevant function of acidity is, not the acid concentration, but the Hammett function h_0, and perhaps also the function h_+. In water, when h_0 and $[H^+]$ diverge, h_0 always rises the faster, and in a certain range will

[1] van Loon, *Rec. Trav. chim.*, 1904, **23**, 62.
[2] Hammond and Shine, *J. Amer. Chem. Soc.*, 1950, **72**, 220.
[3] Carlin, Nelb, and Odioso, *ibid.*, 1951, **73**, 1002.
[4] Carlin and Odioso, *ibid.*, 1954, **76**, 100, 2345.
[5] Croce and Gettler, *ibid.*,, 1953, **75**, 874.

rise somewhat similarly to $[H^+]^2$. We do not know how the acidity function of hydrogen chloride varies with concentration in any of the alcoholic media used in the foregoing investigations. Hence we do not know the region of concentration in which h_0 diverges from $[H^+]$, or resembles $[H^+]^2$, though it might well lie quite low. Thus it seems possible to overestimate on this account the kinetic order in acid. It is certain that, at concentrations of tenths molar, activity coefficients will not depend on 1 : 1-electrolytes simply through their concentrations, independently of their nature: at such concentrations, " ionic strength " will have no clear meaning for kinetics, and, in particular, activity coefficients will not remain constant while hydrogen chloride is replaced by sodium perchlorate or lithium chloride. A still more elementary difficulty is that we do not know above what concentrations hydrogen chloride ceases to be completely ionised in the alcoholic media, though this also probably happens at somewhat low concentrations.

FIG. 1. *Rearrangement of hydrazobenzene by perchloric acid in 60% aqueous dioxan at 0°. Logarithmic plot of the rate constant* versus *the acid concentration. The slope of the straight line is 2·0.*

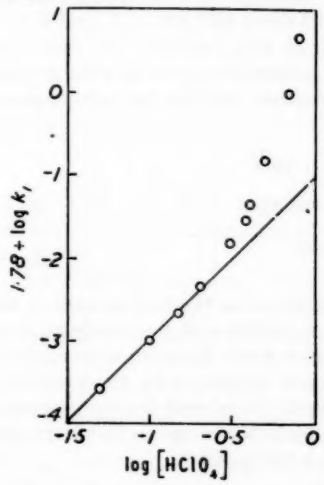
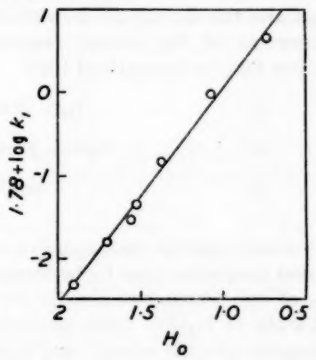


FIG. 2. *Rearrangement of hydrazobenzene by perchloric acid in 60% aqueous dioxan at 0°. Plot of the logarithm of the rate constant* versus *Hammett's* $H_0 = -\log h_0$. *The slope of the line is 2·6.*



Incomplete ionisation, if it were considerable, would lead to an underestimation of the kinetic order in acid.

These difficulties could be overcome by investigating the catalysis of the rearrangement by a strong acid in a medium in which its Hammett functions are known. Most acidity functions have been determined, nearly all of them h_0 functions, for mixtures of strong acids with water. But for very many organic chemical reactions, including the benzidine rearrangement, water is not a convenient, or even a practicable, solvent. As a step towards meeting this general difficulty in the investigation of acid-catalysed organic reactions, a number of tables of the function h_0 have been constructed in these laboratories for strong acids in dioxan–water mixtures. They will be published soon (by Bunton, Ley, Rhind-Tutt, and Vernon); but one of them, that relating to perchloric acid in 60% aqueous dioxan at 0°, has found service in the present investigation.

Results.—First-order rate constants for the rearrangement of hydrazobenzene under catalysis by perchloric acid in 60% aqueous dioxan at 0° are given in Table 1. Their significance is shown in Figs. 1 and 2.

As Fig. 1 shows, the rate of rearrangement at low acidities follows the square of the acid concentration to acidities above 0·1M. However, near 0·2M the rate begins to rise

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considerably faster than the square of the acid concentration. Nevertheless, as Fig. 2 shows, the logarithm of the rate continues to rise linearly with the Hammett function $H_0 = -\log h_0$ up to much higher concentrations, indeed up to the highest for which rates could be measured.

TABLE 1.—*First-order rate-constants* (k_1 *in sec.*$^{-1}$) *for the rearrangement of hydrazobenzene in the presence of perchloric acid in a mixture of* 60 *vols. of dioxan with* 40 *vols. of water at* 0°.

[$HClO_4$] (M)	0·050	0·101	0·151	0·200	0·304	0·383	0·406	0·500	0·700	1·000
10^4k_1	0·427	1·63	3·53	7·67	25·5	47·5	74·2	248	1600	7350

Discussion.—Our results clearly substantiate previous suggestions that the rearrangement goes through the second conjugate acid of hydrazobenzene. However, several mechanisms of acid catalysis will satisfy that condition. The most worthy of consideration seem to be four, which all assume a rapid and reversible formation of the first conjugate acid of hydrazobenzene. With respect to the formation of the second conjugate acid, two of the four are mechanisms of specific hydrogen-ion catalysis, and two are mechanisms of general acid catalysis. We shall label them *SH*, *SH'*, *GA*, and *GA'*.

The first specific hydrogen-ion mechanism assumes that, not only the first conjugate acid, but also the second, are formed in rapid pre-equilibria, the slow step occurring in the rearrangement of the second conjutate acid. Writing Hz for hydrazobenzene, this mechanism may be formulated thus:

(1) $H_3O^+ + Hz \underset{\text{Fast}}{\rightleftharpoons} HzH^+ + H_2O$

(2) $H_3O^+ + HzH^+ \underset{\text{Fast}}{\rightleftharpoons} HzH_2^{++} + H_2O$

(3) $HzH_2^{++} \xrightarrow[\text{Slow}]{} \text{Products}$

. . . . . (*SH*)

The second specific hydrogen-ion mechanism differs from the first in that it assumes the second conjugate acid to be formed by the slow addition of a pre-activated proton, that is, of one which has already escaped from its normal situation of binding in the ground state of H_3O^+. Such pre-activation has been suggested for the protonation of carbon–carbon double bonds,[6] and it might conceivably be needed for the protonation of such a very weak base as the first conjugate acid of hydrazobenzene. The rearrangement of the second conjugate acid would now be taken as a fast process:

(1) $H_3O^+ + Hz \underset{\text{Fast}}{\rightleftharpoons} HzH^+ + H_2O$

(2) $H_3O^+ \underset{\text{Fast}}{\rightleftharpoons} H^+ + H_2O$

(3) $H^+ + HzH^+ \xrightarrow[\text{Slow}]{} HzH_2^{++}$

(4) $HzH_2^{++} \xrightarrow[\text{Fast}]{} \text{Products}$

. . . . . (*SH'*)

With the usual assumptions underlying the kinetic use of Hammett functions,[7] both these mechanisms lead to the approximate rate equation:

$$\text{Rate} \propto h_0h_+[\text{Hz}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (a)$$

The third mechanism assumes the second conjugate acid to be formed by a slow protonation effected by the ordinary solvated hydrogen ion. This mechanism is in part one of general acid catalysis, because, although the transition state contains only the proton from the first protonation, it contains the whole acid molecule, H_3O^+, involved in

[6] de la Mare, Hughes, Ingold, and Pocker, *J.*, 1954, 2930.
[7] Hammett, "Physical Organic Chemistry," McGraw-Hill, London, 1940, p. 273.

the second protonation. Here also the rearrangement of the second conjugate acid is a fast process :

$$\left.\begin{array}{ll} (1) & H_3O^+ + Hz \underset{\text{Fast}}{\rightleftharpoons} HzH^+ + H_2O \\ (2) & H_3O^+ + HzH^+ \xrightarrow[\text{Slow}]{} HzH_2^{++} + H_2O \\ (3) & HzH_2^{++} \xrightarrow[\text{Fast}]{} \text{Products} \end{array}\right\} \quad \ldots\ldots\ldots \quad (GA)$$

The fourth mechanism assumes that the second protonation is rapid and reversible, but that the rearrangement of the second conjugate acid depends on the slow extraction of a proton, presumably from carbon, by water acting as a base. This is also general acid catalysis, because the transition state includes the equivalent of a molecule of the acid H_3O^+, even though it has been acquired a piece at a time :

$$\left.\begin{array}{ll} (1 & H_3O^+ + Hz \underset{\text{Fast}}{\rightleftharpoons} HzH^+ + H_2O \\ (2) & H_3O^+ + HzH^+ \underset{\text{Fast}}{\rightleftharpoons} HzH_2^{++} + H_2O \\ (3) & H_2O + HzH_2^{++} \xrightarrow[\text{Slow}]{} \text{Products} \end{array}\right\} \quad \ldots\ldots\ldots \quad (GA')$$

Again with the usual assumptions underlying the use of Hammett functions in kinetics, and, in particular, acceptance of the Zucker–Hammett hypothesis,[7] both general acid mechanisms lead to the approximate rate-equation,

$$\text{Rate} \propto h_0[H_3O^+][[Hz] \quad \ldots\ldots\ldots \quad (b)$$

Thus the distinction on which the present results bear is essentially that between specific hydrogen-ion mechanisms requiring equation (*a*), and general acid mechanisms requiring equation (*b*).

This last statement requires a reservation concerning mechanism *GA*. For Long and Paul have suggested [8] that, in reactions depending on slow proton-transfers from strong acids, the Zucker–Hammett hypothesis may be inapplicable, because the H_2O-portion of the solvated hydrogen ion is not sufficiently deeply implicated in the transition state to influence its activity coefficient as it influences that of the initial state. If this were so, the kinetic equation would be (*a*), and not (*b*). But if it were so, we would prefer to re-classify the reaction as one of specific hydrogen-ion catalysis, and to represent in some explicit way, perhaps somewhat as shown for reaction *SH'*, the effective disengagement from water of the proton that is to enter the transition state. With this understanding, we may retain our classification of mechanisms into specific hydrogen-ion and general acid mechanisms, having the kinetic equations (*a*) and (*b*), respectively.

In seeking to compare our rates with equations (*a*) and (*b*), we meet the difficulty that we possess a Table of values of h_0, but not of h_+. That is why the conclusion, which is reached below, takes the slightly unsymmetrical form that the data exclude equation (*b*), but might be consistent with equation (*a*).

As to equation (*b*), we know that, as h_0 rises, $[H^+]$ drops increasingly below it. Hence equation (*b*) requires that the points in Fig. 2 should describe a curve bending over strongly towards the H_0 axis. This is not observed.

As to equation (*a*), we know that, as $[H^+]$ rises, h_0 will rise increasingly above it; and it is probable that h_+ will also rise above it, rather similarly. If any lack of proportionality between h_0 and h_+ could be neglected, so that equation (*a*) could be approximated to the equation,* Rate $\propto h_0^2[Hz]$, then the slope of the plot in Fig. 2 would be required to

* *Added, February 27th*, 1957.—Bonner and Lockhart (*J.*, 1957, 364) showed that for aqueous sulphuric acid H_0 and H_+ differ at most by a small constant. If the same is true of perchloric acid in aqueous dioxan, then h_+ can indeed be replaced by h_0 in eqn. (*a*).

[8] F. A. Long and M. A. Paul, forthcoming paper in *Chem. Reviews*. Professor Long was very kind in allowing us to see this paper in manuscript.

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be 2. In the acid concentration range 0·2—1·0M, covered in Fig. 2, the actual slope is 2·6, though at low acidities, from 0·1M downwards, as will be clear from Fig. 1, the slope must fall to 2. Now the literature contains rate data [8] for a number of reactions that depend on single pre-equilibrium protonations; and for these reactions, linear plots, analogous to that of Fig. 2, have been obtained. The slopes are not all exactly 1, but vary from case to case, between 0·86 and 1·25. These deviations from the theoretical slope of 1 are ascribed [8] to "specific effects," that is, to the invalidity of the assumption, inherent in the use of Hammett functions, that the ratio of the activity coefficients of two species differing in composition only by a proton is the same for all pairs of species. The fact that our slope for double protonation is rather greater than twice the largest of the slopes observed for single protonation might be due either to a steeper increase of h_+ than of h_0 with increasing acidity, or to greater specific effects in the double protonation.

The conclusion to be drawn from this work is that the benzidine rearrangement does indeed involve the second conjugate acid of hydrazobenzene, and that the relative rates of the successive processes form a pattern consistent with specific hydrogen-ion catalysis, but not with general acid catalysis. We cannot distinguish between the more conventional specific hydrogen-ion scheme labelled *SH*, and the less usual active-proton scheme labelled *SH'*.

(2) *Hydrogen-isotope Dependence of the Rate of the Benzidine Rearrangement*

Cohen and Hammond [9] examined the kinetics of the rearrangement of hydrazobenzene in aqueous ethanol in the presence of acids ranging in strength from formic to cyanoacetic, in concentrations up to 2·5M, with the addition of their sodium salts, as well as of either lithium perchlorate or potassium chloride in order to make up the so-called ionic strength. They interpreted their results as pointing to general acid catalysis, although their catalytic coefficients could not be fitted to a Brönsted relation. The difficulty in interpreting such work is that the great medium changes must profoundly modify all activity coefficients.

Since Cohen and Hammond's conclusion is not that reached in the preceding Section, it seemed desirable to seek evidence by an independent method. The obvious method was the study of hydrogen-isotope effects.

On the assumption, in agreement with Cohen and Hammond, that the question of general acid catalysis could be seriously entertained only with respect to the second step of protonation, the two mechanisms which fall within the scope of such catalysis are those labelled *GA* and *GA'* in Section 1. Now Hammond and Grundemeier [10] took the first step in the application of hydrogen-isotopic methods by introducing deuterium into the substrate: they showed that *para*-deuterated hydrazobenzene does not rearrange significantly more slowly than does the undeuterated compound. It follows that extraction of a benzenoid proton is not rate-controlling, *i.e.*, that mechanism *GA'* is inapplicable. Thus mechanism *GA* remains the only acceptable expression of the theory of general acid catalysis.

Between mechanism *GA*, on the one hand, and the two mechanisms, *SH* and *SH'*, of specific hydrogen-ion catalysis, on the other, a strong distinction can be drawn with respect to the expected kinetic effects of hydrogen-isotopic substitution *in the solvent*. The method is well known,[11] and its two simple principles are that D_3O^+ in D_2O is a stronger acid than is H_3O^+ in H_2O, and that D^+ is transferred from, or to form, D_3O^+ more slowly than is H^+ from, or to form, H_3O^+. Thus every pre-equilibrium step involving destruction of a solvated hydrogen ion makes a reaction go faster in a deuterium than in a protium solvent, whilst every step of slow destruction or formation of a solvated hydrogen ion

[9] Cohen and Hammond, *J. Amer. Chem. Soc.*, 1953, **75**, 880.
[10] Hammond and Grundemeier, *ibid.*, 1955, **77**, 2444.
[11] Bell, "Acid–Base Catalysis," Clarendon Press, Oxford, 1949, p. 143.

makes a reaction go more slowly in the deuterium solvent. Recorded factors of acceleration in deuterium water for single pre-equilibrium steps are often about 2, the largest one known to us being 2·7. Factors of retardation arising from a single slow transfer can range from not much above 1, to considerably more than 2.

The following is an analysis of the effects, to be expected from a change from a protium to a deuterium solvent, on rate by each of the mechanisms set out in Section 1. The figures refer to the numbers of the stages, and the signs $>$ and $\lesssim$ represent one-stage factors of acceleration and retardation, respectively, in the deuterium solvent :

(*SH*)	(1)	D > H, (2) D > H, (3) —	Overall D $\gg$ H
(*SH'*)	(1)	D > H, (2) D > H, (3) —, (4) —	,, D $\gg$ H
(*GA*)	(1)	D > H, (2) D $\lesssim$ H, (3) —	,, D $\gtrsim$ H
(*GA'*)	(1)	D > H, (2) D > H, (3) D $\lesssim$ H	,, D > H

Evidently, the specific hydrogen-ion mechanisms *SH* and *SH'* should distinguish themselves by showing a large acceleration (*e.g.*, by a factor 4) in a deuterium solvent. The general acid mechanism *GA* should have a not much greater rate in a deuterium than in a protium solvent. The only mechanism for which an intermediate behaviour is predicted, which might have led to difficulty of identification, is mechanism *GA'*; but this has already been excluded by Hammond and Grundemeier's investigation.

Results and Discussion.—The results of our comparative measurements of the rate of rearrangement of hydrazobenzene under catalysis by perchloric acid in media made with ordinary water and with deuterium water are assembled in Table 2. They show that the reaction goes four times faster in the deuterium than in the protium solvent. This is an unprecedentedly large factor of increase, one which it would seem impossible to understand, except on the basis of two pre-equilibrium proton-transfers.

TABLE 2. *Comparison of first-order rate constants* (k_1 *in sec.*$^{-1}$) *in the rearrangement of hydrazobenzene in the presence of perchloric acid* (*concns.* M) *in mixtures of* 60 *vols. of dioxan with* 40 *vols. of either water or deuterium oxide at* 0°.

H_2O–dioxan		D_2O–dioxan		Comparison			
[$HClO_4$]	10^5k_1	[$DClO_4$]	10^5k_1	[Acid]	10^5k_H	10^5k_D	k_D/k_H
0·101	1·63	0·104	6·40	0·100	1·60	5·89	3·7
0·200	7·67	0·195	29·8	0·200	7·67	31·3	4·1
						Mean	3·9

We conclude that the mechanism of rearrangement of hydrazobenzene in our conditions cannot be one of general acid catalysis, and is very reasonably regarded as one of specific hydrogen-ion catalysis, though we still cannot decide between mechanisms *SH* and *SH'*, *i.e.*, between pre-equilibrium proton-transfer and pre-equilibrium proton-desolvation.

(3) *Kinetic Dependence of the Semidine Rearrangement on Acidity*

The kinetics of the semidine rearrangement have not previously been determined, although Dewar [12] deduced from a pre-conception concerning the mechanism of benzidine and semidine rearrangements that the latter should distinguish themselves from the former in that semidine changes should show only a first-order kinetic dependence on acid. We have examined the matter in the example of the rearrangement of 4 : 4'-dimethylhydrazobenzene to the *o*-semidine, under catalysis by perchloric acid, in 60% aqueous dioxan at 0°.

[12] Dewar, *Ann. Reports*, 1951, **48**, 126.

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Results and Discussion.—The reaction is fast, and we were accordingly restricted to acidities so low that there is no clear distinction between $[H^+]$, and h_0 or h_+. Therefore we describe our results in terms of the concentration $[H^+]$. The results themselves are in Table 3, and a logarithmic plot of first-order rate constants *versus* acid concentrations is shown in Fig. 3, in which the straight line has a slope of 2·0.

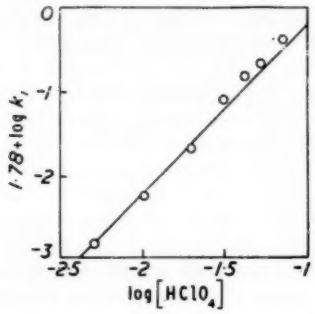

FIG. 3. *Rearrangement of* 4 : 4′*-dimethylhydrazobenzene by perchloric acid in* 60% *aqueous dioxan at* 0°. *Logarithmic plot of the rate constant* versus *the acid concentration. The slope of the line is* 2·0.

From these results it is clear that, contrary to prediction from Dewar's theory, the semidine rearrangement is, not only of first order in the hydrazobenzene, but also of second order in acid. It thus has the same kinetic form as the benzidine rearrangement.

TABLE 3. *First-order rate constants* (k_2 *in sec.*$^{-1}$) *for the rearrangement of* 4 : 4′*-dimethylhydrazobenzene in a solution of perchloric acid* (M) *in a mixture of* 60 *vols. of dioxan with* 40 *vols. of water at* 0°.

$[HClO_4]$ (M)	0·0051	0·0104	0·0200	0·0309
10^5k_1	2·33	8·93	33·3	135·5
$[HClO_4]$ (M)		0·0417	0·0515	0·0708
10^5k_1		253	365	722

Although this has been checked only at low acidities, it seems likely that it will apply right up the acidity scale. The semidine rearrangement, like the benzidine rearrangement, takes place by way of the second conjugate acid of the hydrazobenzene.

This conclusion is consistent with the suggestion, contained in Brownstein, Bunton, and Hughes's proposed mechanism [13] of benzidine and semidine rearrangements, that they pursue a common path to, and through, a rate-controlling step, becoming differentiated only later by product-determination in concurrent fast steps. Like the earlier mechanism due to Hughes and Ingold,[14] this new mechanism can accommodate all the facts so far established. Accordingly an attempt is now being made experimentally to distinguish between the two ideas, through the effect of *o*- and *p*-deuteration, particularly the former, on rates and product-ratios, especially the latter.

EXPERIMENTAL

Materials.—Hydrazobenzene, m. p. 125°, and 4 : 4′-dimethylhydrazobenzene, m. p. 133—134°, prepared by alkaline reduction of the appropriate nitro-compounds, were crystallised from aqueous ethanol until almost colourless, and were stored in desiccators under nitrogen. Bindschedler's Green was prepared as described by Dewar.[15] The solvent was prepared by mixing 60 volumes of purified dioxan with 40 of either water or deuterium oxide. Perchloric acid was made up so that its solvent content had these compositions.

Kinetic Methods.—The procedure was essentially that outlined by Dewar [15] and by Hammond and Shine.[2] For the slower runs with hydrazobenzene, separate solutions of this

[13] Brownstein, Bunton, and Hughes, *Chem. and Ind.*, 1956, 981.
[14] Hughes and Ingold, *J.*, 1941, 608.
[15] Dewar, *J.*, 1946, 777.

substance and of perchloric acid were cooled to 0°, and mixed; and then aliquot parts were withdrawn, and added to Bindschedler's Green, the excess of which was subsequently titrated with titanous sulphate. For the faster runs with hydrazobenzene, series of inverted-Y tubes were used. The solutions of hydrazobenzene and of perchloric acid were placed in the separate limbs, cooled to 0°, and mixed by tilting; and the reaction was subsequently stopped by the addition of excess of Bindschedler's Green. All runs with hydrazobenzene gave good first-order rate constants as far as the reaction was followed, in some cases to over 90% of the stoicheiometric total.

The runs with 4 : 4′-dimethylhydrazobenzene were affected by an appreciable reaction between the formed semidine and the dye. For this reason, only about the first 40% of reaction gave good first-order rate-constants, and it became our practice to accept the rate constants deduced from these first portions of the reaction. The procedure now was to titrate the residual hydrazo-compound with Bindschedler's Green directly.

During all these experiments the Bindschedler's Green, which is somewhat unstable in solution, was titrated at frequent intervals with titanous sulphate.

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WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER ST., LONDON, W.C.1. [*Received, December 9th*, 1956.]

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358. *Stability of the Glycosidic Linkages in Carbohydrates.*

By WINIFRED G. WRIGHT.

Lactose, cellobiose, and turanose are almost completely oxidised by periodic acid in 24 hours, with fission of the glycosidic linkage, whereas sodium or potassium periodate attacks only the α-glycollic functions in that time.

A method of detecting the degree of hydrolysis of carbohydrates with mineral acids is indicated, applicable also to keto-sugars, where the reducing groups cannot be estimated in the usual manner with hypoiodite.

COURTOIS and RAMET [1] found lactose to be completely oxidised by periodic acid within four days at room temperature, according to the equation :

$$C_{12}H_{22}O_{11} + 11O = 2CH_2O + 9H{\cdot}CO_2H + CO_2$$

Earlier stages in the oxidation were not recorded. Courtois, Wickstrom, and Le Dizet [2] found that at 0—2° only 8·65 atoms of oxygen were consumed in 15 days. We have found that at room temperature 8·46 equivalents of acid are produced within 24 hours on oxidation with periodic acid, whereas only 2·28 equivs. are produced by the potassium salt (see Table 1 and Fig 3).

Head and Hughes [3] record that with 0·15M-sodium metaperiodate at 20°, cellobiose absorbs five oxygen atoms in 24 hours, and eleven atoms within 50 days. At the same temperature we have found an absorption of ten atoms of oxygen, with the production of 8·56 equivalents of acid, within 23 hours, when the oxidising agent was periodic acid, and an absorption of only 4·67 atoms when it was the potassium salt (0·016M) (Table 3, Fig. 1).

On oxidation with potassium periodate, turanose absorbed 5·5 atoms of oxygen in 48 hours, only the α-glycollic group being attacked in that time, whereas in 24 hours, with periodic acid, 8·36 atoms of oxygen were absorbed with the production of seven equivalents of acid (Fig. 2, Table 4).

[1] Courtois and Ramet, *Bull. Soc. Chim. biol.*, 1947, **29**, 240.
[2] Courtois, Wickstrom, and Le Dizet, *ibid.*, 1952, **34**, 1121.
[3] Head and Hughes, *J.*, 1954, 603.

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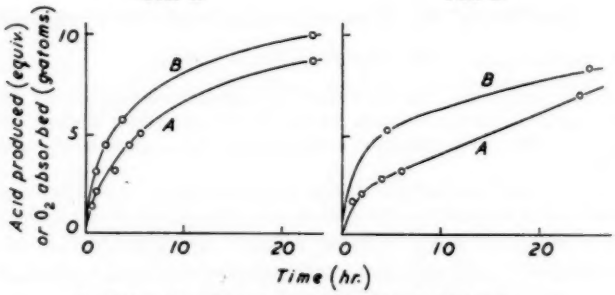
TABLE 1. *Oxidation of lactose.*

Oxidant	Lactose concn. (M)	Time (min.)	Acid produced (equiv.)	After 5 min. in 3% H_2SO_4 at 100° Oxidant	Lactose concn. (M)	Time (min.)	Acid produced (equivs.)
HIO_4, 0·1082N ...	0·00746	50	2·15	HIO_4, 0·1120N ...	0·00197	60	2·25
		80	2·43			75	2·45
		110	2·70			90	2·71
0·1118N ...	0·00761	180	3·30			112	2·80
0·1541N ...	0·00660	270	4·94	KIO_4, 0·0158N ...	0·00325	65	1·31
		390	6·04			120	1·68
		1380	8·46			180	1·98
$NaIO_4$, 0·0733N	0·00593	60	1·67			240	2·05
		90	1·82			300	2·17
		105	1·86			1500	2·28
		128	1·96				
		143	2·03				
		162	2·01				
		177	2·01				

In all these cases, overoxidation is exceedingly slow (negligible in 24 hours) when the salts of periodic acid are used, whereas almost complete oxidation takes place in that time when the free acid is used.

FIG. 1. FIG. 2.



A, Acid produced (equivs.). B, O_2 absorbed (atoms).

FIG. 1. *Oxidation of cellobiose with 0·1027N-periodic acid.*

FIG. 2. *Oxidation of turanose with 0·1216N-periodic acid.*

Oxidation for 24 hours with the potassium salt, and then with the free acid, should give an indication of the presence of 1 : 3- and 1 : 4-bonds in polysaccharides.

The course of the oxidation of turanose is shown in the annexed scheme. The first stage is formation of a formic ester, hydrolysis and subsequent oxidation of which gives rise[4] to the active hydrogen atom, marked *. By stage 6, the glycosidic linkage of the saccharide has become part of a carbonic ester and is then hydrolysed. Eleven oxygen atoms in all are absorbed, with the production of three mols. of formaldehyde, seven of formic acid, and two of carbon dioxide. Essentially the same reaction mechanism would apply to the keto- or pyranose form of the sugar.

The 1 : 4-glycosidic linkage of lactose was not hydrolysed by boiling 3% mineral acid in five minutes, curves representing the course of oxidation with periodic acid before and after treatment with the mineral acid being coincidental (Fig. 3, curve *B*).

Similar results were obtained with raffinose (Fig. 4). The 1 : 2-bond was hydrolysed by boiling 3% mineral acid in five minutes, and, after neutralisation, the mixture was

[4] Sprinson and Chargaff, *J. Biol. Chem.*, 1946, **164**, 433; Huebner, Ames, and Bubl, *J. Amer. Chem. Soc.*, 1946, **68**, 1621.

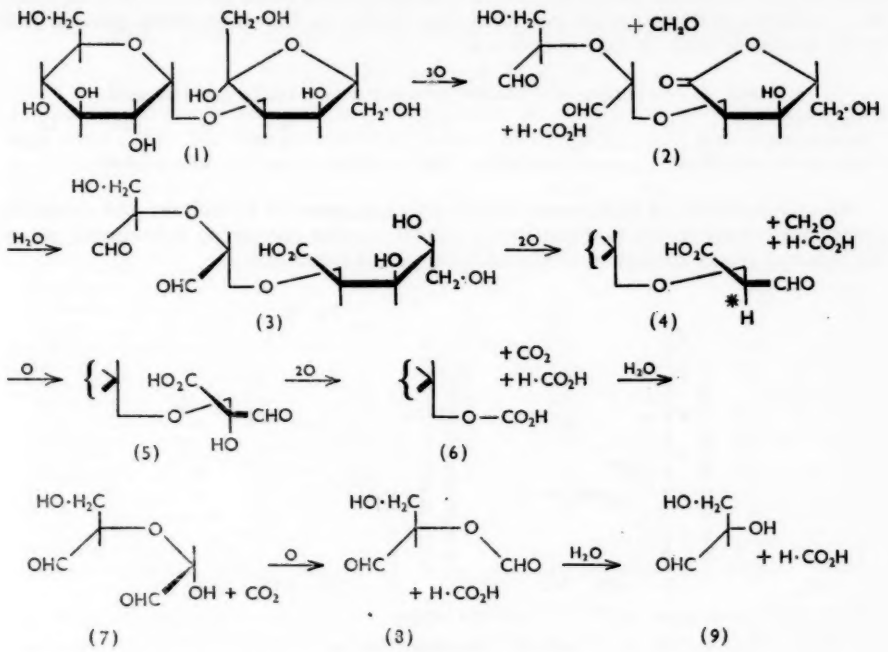


TABLE 2. *Oxidation of raffinose after 5 minutes' hydrolysis by 3% sulphuric acid at 100°.*

Reactants	Time (min.)	O_2 abs. (atoms)	Acid produced (equiv.)	Reactants	Time (min.)	Acid produced (equiv.)
KIO_4, 0·0136N ...	60	—	4·08	HIO_4, 0·1120N	75	5·19
Sugar, 0·00125M	240	—	5·42	Sugar, 0·00118M	90	5·38
	300	—	5·62		130	5·62
	360	8·25	6·02		180	6·13
$NaIO_4$, 0·0473N	120	8·05	—	$NaIO_4$, 0·0733N	150	6·11
Sugar, 0·00109M				Sugar, 0·00071M		

Oxidation of raffinose after 24 hours' hydrolysis by cold 10% sulphuric acid.

Reactants	Time (min.)	O_2 abs. (atoms)	Acid produced (equiv.)
KIO_4, 0·0121N	45	—	3·97
	75	—	4·55
Sugar, 0·00095M	95	—	4·62
	135	7·43	—
	173	—	5·20
	233	—	5·39
	240	7·93	—
	420	8·40	5·95

TABLE 3. *Oxidation of cellobiose with 0·1027N-periodic acid.*

Cellobiose concn. (M)	Time (hr.)	Acid produced (equiv.)	Cellobiose concn. (M)	Time (hr.)	O_2 abs. (atoms)	Acid produced (equiv.)
0·00840	0·5	1·40	0·00786	3·75	5·72	—
	1	2·05		4·5	—	4·41
	3	3·17		5·5	—	5·00
				23	9·98	8·56

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oxidised with potassium periodate. After treatment for 24 hours with cold 10% sulphuric acid, oxidation with potassium periodate gave points on the same curve, proving that the 1 : 6-bond is stable in the stronger acid.

TABLE 4. *Oxidation of* 0·00526M-*turanose with* 0·1027N-*periodic acid.*

Time (hr.)	1	2	4	4·5	6	24	25
O_2 absorbed (atoms)	—	—	—	5·29	—	—	8·36
Acid produced (equiv.)	1·72	2·11	2·80	—	3·30	7·03	—

Any displacement of such curves should give a measure of hydrolysis, and should be particularly useful in the examination of polysaccharides containing keto-sugars, where the reducing groups cannot be estimated by means of hypoiodite.

FIG. 3. FIG. 4.

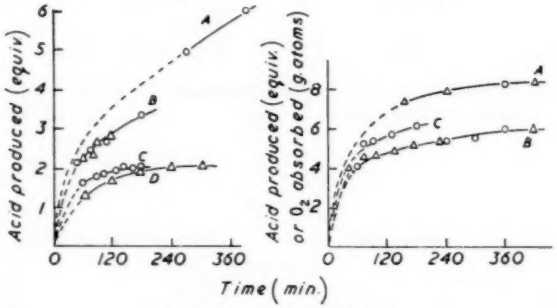

FIG. 3. *Oxidation of lactose.*

A, 0·1541N-HIO_4. *B*, *Points* ○, 0·1541N-HIO_4; *points* △, 0·1120N-HIO_4 *after* 3 *minutes in* 3% H_2SO_4 *at* 100°. *C*, 0·0733N-$NaIO_4$. *D*, 0·0158N-KIO_4 *after* 3 *minutes in* 3% H_2SO_4 *at* 100°.

FIG. 4. *Oxidation of hydrolysed raffinose.*

A, O_2 *absorbed (atoms) with* KIO_4. *B*, *Acid produced with* KIO_4. *In A and B; points* ○, *after hydrolysis with* 3% H_2SO_4. △, *after hydrolysis with* 10% H_2SO_4. *C*, *Acid produced with* HIO_4.

EXPERIMENTAL

The solutions of saccharides and periodate, or periodic acid, were kept in the dark, at constant temperature, samples being withdrawn at intervals, and. after destruction of the excess of periodic acid or periodate with ethylene glycol, were titrated with standard sodium hydroxide, bromothymol-blue being used as an indicator.

Absorption of oxygen was determined by the addition of sulphuric acid and potassium iodide, and titration of the liberated iodine, in the usual manner, with thiosulphate.

When the sugars were treated with mineral acid, the solutions were neutralised with sodium hydroxide before addition of the oxidising agent.

The results are recorded in the Tables and Figures.

The conditions of hydrolysis of lactose (3% acid, 100°, 5 min.) were determined as follows. Treatment of lactose with sodium hypoiodite gave a value of 0·993 CHO group; this was increased only to 1·03 by 10 minutes' previous boiling with 3% sulphuric acid, indicating absence of hydrolysis.

Similarly, after being boiled with 3% sulphuric acid for 5 minutes, raffinose gave, on treatment with hypoiodite, a value of 1·01 CHO groups, indicating fission of the sucrose bond only. After 10 minutes' boiling the value rose to 1·21, and after 30 minutes' to 1·38. One hour's boiling with 10% acid gave a figure of 2·12.

Thanks are offered to the Council for Scientific and Industrial Research for a grant, and to Professor F. L. Warren for his interest.

DEPARTMENT OF CHEMISTRY AND CHEMICAL TECHNOLOGY,
UNIVERSITY OF NATAL, DURBAN.

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359. *Fatty Acids of the Seed Fat of* Pongamia glabra.

By S. P. Pathak and L. M. Dey.

The seed fat of *Pongamia glabra* (family Papilionaceae, order Leguminosae) contains about 40% of oil. This has been examined by Desai *et al.*,[1] by Gupta and Mitra,[2] and again by us. The contents of various component fatty acids are shown in the Table. Our results

	Whole fat			Excluding unesterifiable matter			
Acid	Group *A* (% w/w)	Group *B* (% w/w)	Total (% w/w)	Total (mol. %)	Total (% w/w)	Ref. 1 (% w/w)	Ref. 2 (% w/w)
Myristic	—	—	—	—	—	—	1·6
Palmitic	6·2	0·1	6·3	7·1	6·3	6·6	7·9
Stearic	8·0	0·9	8·9	9·1	8·9	2·4	3·7
Arachidic	2·2	—	2·2	2·0	2·2	4·7	2·5
Behenic	5·3	—	5·3	4·5	5·3	—	4·2
Lignoceric	2·0	—	2·0	1·5	2·0	3·5	1·1
Hexadecanoic	0·4	0·2	0·6	0·7	0·6	—	—
Oleic	1·3	44·9	46·2	47·3	46·5	71·3	6·2·1
Linoleic	—	18·1	18·1	18·6	18·2	10·8	11·9
Linolenic	—	—	—	—	—	—	5·0
Eicosenoic	0·3	9·2	9·5	8·9	9·6	—	—
C_{22} (− 2H)	0·2	—	0·2	0·2	0·2	—	—
C_{24} (− 2H)	0·2	—	0·2	0·1	0·2	—	—
Unsaponifiable	0·1	0·4	0·5	—	—	—	—
Total saturated					17·9	24·7	21·0
Total unsaturated					82·1	75·3	79·0

are in broad agreement with those already reported [1,2] of the saturated acids; behenic acid was not found by Desai *et al.*, but Gupta and Mitra, like us, have found it, and it was also isolated by Manjunath and Rao.[3] Among the unsaturated acids, linolenic acid was reported by Gupta and Mitra, but not by Desai *et al.* or us, and eicosenoic, docosenoic, and tetracosenoic acids, which were not found by the previous authors, were found by us.

The results are in line with those from other members of the Family. Eicosenoic acid has been reported (2—9%) in fats from *Macadamia ternifolia*,[4] *Nephelium lappaccum*,[5] *Corchorus capsularis*,[6] and *Erythrina christogalli*.[7]

Experimental. The oil was extracted from the kernels, of which it formed 39·4%, with hot acetone. Its acid value was 2·1, saponification equivalent 289·3, and iodine value 79·4. It was esterified, unsaponifiable matter was removed, and the acids recovered as usual. The mixed acids were resolved by the modified Twitchell lead-salt method [8] into two groups: *A* (26·2%), mainly solid (iodine value 8·2), and *B* (73·8%), mainly liquid (iodine value 109·6).

Each group was separately converted into the methyl esters, and fractionated in an efficient electrically heated column at 0·1 mm., the saponification equivalent and iodine value of each fraction being determined. The composition of the fat was determined by Hilditch's method.[9] The absence of linolenic acid was established by the hexabromide test. The results are contained in the Table.

Department of Industrial Chemistry,
Hindu University, Banaras, India.

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[1] Desai, Sudborough, and Watson, *J. Indian Inst. Sci.*, 1923, **6**, 93.
[2] Gupta and Mitra, *J. Indian Chem. Soc.*, 1953, **30**, 781.
[3] Manjunath and Rao, *ibid.*, 1938, **15**, 653.
[4] Bridge and Hilditch, *J.*, 1950, 2396.
[5] Hilditch and Stainsby, *J. Soc. Chem. Ind.*, 1934, **53**, 197 T.
[6] Meara and Sen, *J. Sci. Food Agric.*, 1952, **5**, 237.
[7] Cataneo, *Anal. Asoc. quím. argentina*, 1945, **33**, 5.
[8] Hilditch, "The chemical composition of natural fats," Chapman and Hall, London, 2nd edn., 1947, p. 468.
[9] Hilditch, ref. 8, pp. 505—510.

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360. *Preparation of Glycol Monoesters of Fatty Acids with the Use of Boron Intermediates.*

By L. Hartman.

The preparation of ethylene glycol monoesters of fatty acids has recently received renewed attention owing to a disagreement on the best method of avoiding diester formation. Verkade and his co-workers [1] prepared pure monoesters by protecting one hydroxyl group of the glycol with the triphenylmethyl group which was removed after acylation. Baer [2] suggested, however, that direct acylation of the glycol in an appropriate solvent mixture is preferable since the triphenylmethyl compound tends to contaminate the final product, which was denied by van Gijzen and Verkade.[3] In view of this controversy Bevan, Malkin, and Smith [4] worked out a procedure based on the acylation of ethylene iodohydrin followed by refluxing of the iodoethyl ester with alcoholic silver nitrite, whereby iodine is replaced by hydroxyl.

All these methods require thorough purification of reagents and anhydrous conditions owing to the use of acid chlorides. In comparison, Hilditch and Rigg's method [5] of direct esterification of fatty acids with a large excess of glycol (up to 10 mol.) in phenol solution is much simpler. Unfortunately phenol apparently enters into the reaction, which would explain the low melting points recorded by Hilditch and Rigg for their products. The search for an alternative method led to the selection of tri-(2-hydroxyethyl) orthoborate $B(O{\cdot}CH_2{\cdot}CH_2{\cdot}OH)_3$ as an intermediate in the synthesis of monoesters. The preparation of this orthoborate from ethylene glycol and boron trichloride [6] is inconvenient, but it was found that heating boric acid with 3 mols of the glycol *in vacuo* at 80—90° gave a product of sufficient purity. Fatty acids were soluble in, and reacted readily with, this borate at 100° in the presence of toluene-*p*-sulphonic acid. The resulting mixed ester yielded, on hydrolysis with water, the 2-hydroxyethyl ester of the fatty acid. Although some free glycol was probably present in the product of the reaction between boric acid and ethylene glycol, very little fatty-acid diester was formed, owing to the preferential esterification of the orthoborate. It was even found that despite the use of a large excess (3·3 mols.) of borate, the esterification led almost exclusively to $B(O{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}OC{\cdot}R)_3$ instead of the expected mixture of mono-, di-, and tri-esters. An excess of borate was needed to reduce the time and temperature of the reaction. Temperatures above 100° resulted in appreciable formation of the diester.

A similar procedure was tried for the preparation of monoglycerides, but proved unsuccessful owing to the complexity of the reaction between glycerol and boric acid.

Experimental.—Materials. Commercial decanoic, lauric, myristic, palmitic, and stearic acid were purified by fractional distillation of their methyl esters and crystallisation. Good-quality ethylene glycol and boric acid of analytical-reagent grade were used.

Tri-(2-hydroxyethyl) orthoborate. Ethylene glycol (12·4 g., 0·2 mole) and boric acid (4·1 g., 0·066 mole) were heated on a water-bath *in vacuo* at 80—90° until evolution of water ceased (10 min.; loss of wt., 3·7 g.; calc., 3·6 g.). The product was a viscous liquid which solidified overnight; it was soluble after melting in chloroform but insoluble in ethyl ether and hydrocarbons. Its boron content was determined by boiling a sample with water under reflux for a few minutes and titrating the boric acid with 0·1N-sodium hydroxide in the presence of mannitol (phenolphthalein) (Found: B, 5·5. Calc. for $C_6H_{15}O_6B$: B, 5·6%). However, the product was not pure. Extraction with a mixture of anhydrous ethyl ether and methyl acetate yielded a liquid fraction containing 0·94% of boron whereas digestion with absolute

[1] Verkade, Tollenaar, and Posthumus, *Rec. Trav. chim.*, 1942, **61**, 373.
[2] Baer, *J. Amer. Chem. Soc.*, 1953, **75**, 5533.
[3] Van Gijzen and Verkade, *Rec. Trav. chim.*, 1954, **73**, 496.
[4] Bevan, Malkin, and Smith, *J.*, 1955, 1043.
[5] Hilditch and Rigg, *J.*, 1935, 1774.
[6] Councler, *Ber.*, 1878, **11**, 1106.

ethanol gave a solid residue containing 10·3% of boron. On the other hand, the infrared absorption spectra of the product and of tri-(2-hydroxyethyl) borate prepared from the glycol and an excess of boron trichloride [6] agreed fairly well and there was no indication of absorption characteristic of free boric acid. (The absorption spectra were scanned over the region 4000—650 cm.$^{-1}$ with a Perkin-Elmer model 21 infrared spectrophotometer.) Thus it could be assumed that the product was essentially the borate $B(O{\cdot}CH_2{\cdot}CH_2{\cdot}OH)_3$ containing some free glycol and diborate $B(O{\cdot}CH_2{\cdot}CH_2{\cdot}O)_3B$ (calc. for $C_6H_{12}O_6B_2$: B, 10·7%).

Glycol monopalmitate and other monoesters. Palmitic acid (5·1 g, 0·02 mole) and toluene-*p*-sulphonic acid (0·2 g.) were dissolved in warm tri-(2-hydroxyethyl) borate (12·8 g., 0·066 mole; freshly prepared) and heated on a boiling-water bath for 1 hr. *in vacuo*. The product was swirled with water (50 ml.) to hydrolyse the palmito-boric ester, and the monopalmitate extracted with warm light petroleum (b. p. 40—60°). On cooling, the petroleum extract gave colourless plates of 2-hydroxyethyl palmitate (5 g., 80%), m. p. 52—53° (lit., 52—53°) (Found: C, 72·0; H, 11·9. Calc. for $C_{18}H_{36}O_3$: C, 71·9; H, 12·0%).

Similarly were obtained the *decanoate*, m. p. 16—17° (Found: C, 66·4; H, 11·1. $C_{12}H_{24}O_3$ requires C, 66·7; H, 11·2%), laurate, m. p. 32—32·5° (lit., 31—32°) (Found: C, 68·7; H, 11·4. Calc. for $C_{14}H_{28}O_3$: C, 68·8; H, 11·5%), myristate, m. p. 42·5—43·5° (lit., 43—43·5°) (Found: C, 70·6; H, 11·8. Calc. for $C_{16}H_{32}O_3$: C, 70·5; H, 11·8%), and stearate, m. p. 60—61° (lit., 60—61°) (Found: C, 73·2; H, 12·0. Calc. for $C_{20}H_{40}O_3$: C, 73·1; H, 12·3%).

These monoesters can be also prepared in a single-stage process by heating all the ingredients *in vacuo* for 1 hr. at 90—100°. The danger of diester formation is not great since fatty acids and the glycol are not miscible at 100°, and the glycol reacts at this temperature much faster with boric acid than with fatty acids. However, the removal of water proceeds more smoothly in a two-stage reaction.

The mixed ester of boric and palmitic acid was isolated in a separate sample by extracting the mixture with light petroleum (b. p. 40—60°) in which the glycol and the borate are practically insoluble. From the petroleum solution a white semicrystalline substance was recovered which melted at 49—50° (3·15 g. from 2·56 g. of palmitic acid). This substance was dissolved in ethyl ether and washed three times with small portions of water to effect hydrolysis. Boric acid was determined in the aqueous extract by titration as above (Found: B, 1·3. Calc. for $B(O{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}OC{\cdot}C_{15}H_{31})_3$: B, 1·2%). The yield calculated on this basis (3·02 g.) also agreed well with that obtained (3·15 g.). From the ethereal solution 2-hydroxyethyl palmitate, m. p. 52—53°, was recovered.

It was found that triglycol orthoborate can also be esterified with fatty acid chlorides in chloroform at room temperature by using pyridine or quinoline as catalyst. This procedure, however, has no advantage over esterification with fatty acids and is much more time-consuming. It could be used for steam-volatile fatty acids to avoid losses which would occur during heating *in vacuo*.

The infrared absorption spectra of the borates and boric acid were measured by Dr. B. Cleverley, of Dominion Laboratory, Department of Scientific and Industrial Research.

FATS RESEARCH LABORATORY, DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH, WELLINGTON, NEW ZEALAND. [*Received, September 26th*, 1956.]

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361. *The Isolation of* 5-O-α-L-*Arabopyranosyl*-L-*arabinose from Partly Degraded Gums of* Virgilia *Species.*

By A. M. STEPHEN.

WHILE studying the acid hydrolysis of the polysaccharide gums obtained as exudates from the bark of *Virgilia oroboides* and of *V. divaricata* Adamson (the South African "Keurboom"; family, Leguminosae), it was observed that within a few hours of commencing hydrolysis of either gum with 0·01N-sulphuric acid at 95° there was produced, in addition to much arabinose and traces of rhamnose, galactose, and a number of oligosaccharides, a disaccharide whose rate of movement on paper chromatograms was just

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slower than that of galactose. This substance showed a pink spot when the chromatogram was sprayed with aniline hydrogen oxalate or *p*-anisidine hydrochloride, and, on isolation and hydrolysis, gave L-arabinose only. There was maximum production of the disaccharide after about 5 hr., hydrolysis to arabinose occurring during the following 20 hr.

The disaccharide was isolated as a hygroscopic white powder,* $[\alpha]_D$ −14°, from *V. oroboides* gum after hydrolysis for 6 hr., followed by column chromatography on cellulose [1] (aqueous butanol as solvent) and elution from charcoal–Celite [2] (with 5% aqueous ethanol), a yield of about 4% being obtained. A phenylosazone (m. p. 200°; *M* 472, by its absorption [3] at 394 mμ) was prepared, and its oxidation with periodate by the method of Hough, Powell, and Woods [4] gave the 1 : 2-bisphenylhydrazone of mesoxalic dialdehyde, but no formaldehyde (result published by courtesy of Dr. L. Hough). The relatively slow hydrolysis of the disaccharide indicating a pyranosyl structure for the non-reducing unit, the compound appeared to be 5-*O*-α-L-arabopyranosyl-L-arabinose : the anomeric configuration follows from consideration of Hudson's rules.[5] Methylation of the disaccharide afforded a hexa-*O*-methyl derivative, $[\alpha]_D$ −16°, which on acid hydrolysis gave the expected equimolecular mixture of 2 : 3 : 4-tri-*O*-methyl-L-arabinose and 2 : 3-di-*O*-methyl-L-arabinose.

The new disaccharide is the third L-arabopyranosyl-L-arabinose to be reported : the β : 3-linked compound has been isolated after hydrolysis of a number of natural products [6-10] and after acid reversion of L-arabinose,[11] while more recently the β : 4-linked isomer has been shown (tentatively) to be a minor acid reversion product of L-arabinose.[12] In addition, 5-*O*-β-D-xylopyranosyl-L-arabinose has been detected among the hydrolysis products of peach and cholla gums,[7] and this differs from the disaccharide now reported only in the configuration of $C_{(4)}$ of the non-reducing end of the molecule.

It is improbable that the disaccharide produced from these two gums obtained from *Virgilia* spp. should be a reversion product, since the behaviour on acid hydrolysis of the gums, involving rapid splitting of a furanoside bond followed by gradual hydrolysis of the arabopyranosyl moiety of the resulting disaccharide, is fully consistent with a linkage in the gum through $C_{(5)}$ of an arabinose residue. Acid reversion of 5-*O*-α-L-arabopyranosyl-L-arabinose has in fact been brought about by evaporating a concentrated solution in the presence of acid : there was produced a polymer (*ca.* 6 arabinose residues; $[\alpha]_D$ −8°; immobile in the acid and basic chromatographic tanks), which when heated during 6 hr. with 0·01N-sulphuric acid released the disaccharide and no other product in observable quantity, apart from a trace of arabinose. Nevertheless, the gums must be hydrolysed after methylation to establish the mode of bonding of the arabinose residues.

Experimental.—Specific rotations were measured in water. The chromatographic tanks contained butan-1-ol–ethanol–water (4 : 1 : 5, upper layer), ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4), and butan-1-ol–pyridine–water (9 : 2 : 2). R_{gal} and R_G values are relative to D-galactose and 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose, respectively. Paper ionophoresis was carried out for 5 hr. at 700 V and 18 mA, in alkaline borate buffer; [13] the M_G value is relative to D-glucose.

* On being stored, the solid absorbed moisture and crystallised in elongated prisms with blunt ends.

[1] Hough, Jones, and Wadman, *J.*, 1949, 2511.
[2] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.
[3] Barry, McCormick, and Mitchell, *J.*, 1955, 222.
[4] Hough, Powell, and Woods, *J.*, 1956, 4799.
[5] Hudson, *J. Amer. Chem. Soc.*, 1909, **31**, 66; 1916, **38**, 1566.
[6] Jones, *J.*, 1953, 1672.
[7] Andrews, Ball, and Jones, *J.*, 1953, 4090.
[8] Andrews and Jones, *J.*, 1954, 4134.
[9] *Idem*, *J.*, 1955, 583.
[10] Charlson, Nunn, and Stephen, *J.*, 1955, 1428.
[11] Ball, Jones, and Nicholson, Amer. Chem. Soc. Meeting, Minneapolis, Sept. 1955, Abs. Papers, 7*D*.
[12] Ball, Jones, Nicholson, and Painter, TAPPI, 1956, **39**, 438.
[13] Foster, *J.*, 1953, 982.

Isolation. *Virgilia oroboides* gum, collected at Kirstenbosch Botanical Gardens, Cape Town, in late summer (through the courtesy of Professor H. B. Rycroft), was dissolved in water and precipitated in the acid form by pouring an aqueous solution into 0·1N-ethanolic hydrochloric acid, then washed with ethanol and acetone, and dried. A portion of the mother liquors was neutralised and evaporated, yielding a negligible quantity of carbohydrate material which included galactose, arabinose, and numerous oligosaccharides. The gum acid (75 g.) was heated with 0·01N-sulphuric acid (1 l.) at 95° for 6 hr., the solution was cooled, neutralised ($BaCO_3$), and centrifuged, and then concentrated at 45° *in vacuo*. On pouring the clear liquid into excess of methanol, there was obtained the partly-degraded polysaccharide (as barium salt) together with a mixture of sugars in solution. The latter, after concentration to a syrup, was de-ionised with Amberlite resins IR-120(H) and IR-4B(OH) to give a syrup from which chromatographically pure L-arabinose (5·5 g.) crystallised rapidly (after one recrystallisation this had m. p. and mixed m. p. 155—156°, $[\alpha]_D^{20}$ +100°; benzoylhydrazone, m. p. 209°). The syrupy mixture, after removal of the arabinose, was passed through a succession of cellulose and charcoal–Celite columns, whereby more arabinose (9·4 g.), a number of oligosaccharides (1·0 g.), traces of rhamnose and galactose, and a disaccharide (3·3 g.) were separated. This disaccharide had $[\alpha]_D^{20}$ −14° (*c* 1·5); R_{gal} 0·85 (acid tank), 0·90 (basic tank), 0·92 (neutral tank); M_G 0·7; reducing power towards hypoiodite,[14] 0·5 of that of L-arabinose.

Phenylosazone of the disaccharide. On treatment in aqueous solution with phenylhydrazine and acetic acid for 3 hr. at 75°, the disaccharide formed a *phenylosazone* (bright-yellow, elongated prisms from aqueous ethanol), m. p. 198—200° (Kofler block) (Found: C, 55·1; H, 6·1. $C_{22}H_{28}O_7N_4,H_2O$ requires C, 55·2; H, 6·3%); $\lambda_{max.}$ in 95% ethanol: 256 (ε 19,150), 308 (ε 10,580), and 394 mμ (ε 19,840). No trace of L-arabinosazone, which might have been formed by cleavage, could be detected by circular paper chromatography.[15]

Methylation and hydrolysis. The disaccharide (1·04 g.) was methylated by Haworth's method, isolated by chloroform extraction, and then treated twice with Purdie's reagents; distillation of the *product* at 170°(bath)/0·05 mm. yielded a syrup (0·97 g.), n_D^{20} 1·4615, $[\alpha]_D^{20}$ −16° (*c* 4·6) (Found: OMe, 49·0. $C_{16}H_{30}O_9$ requires OMe, 50·8%). A portion (0·91 g.) was hydrolysed with N-hydrochloric acid (20 c.c.) on the boiling-water bath for 2 hr., during which time $[\alpha]_D$ rose rapidly to a final value of +104°. Neutralisation with silver carbonate, followed by removal of silver ion from the filtrate by hydrogen sulphide, filtration, and evaporation, yielded a mixture (0·88 g.) of two methylated sugars which were separated by cellulose-column chromatography, water-saturated butan-1-ol (3 parts) and light petroleum (b. p. 100—120°; 7 parts) being used. There were produced: (i) 2 : 3 : 4-tri-*O*-methyl-L-arabinose (0·43 g.), $[\alpha]_D^{20}$ +120° (*c* 0·86), R_G 0·75 (neutral tank) (Found: OMe, 47·0. Calc. for $C_8H_{16}O_5$: OMe, 48·4%), identified by conversion, after bromine oxidation, into the phenylhydrazide of 2 : 3 : 4-tri-*O*-methyl-L-arabonic acid, m. p. 158° (lit., m. p. 156°); and (ii) 2 : 3-di-*O*-methyl-L-arabinose (0·41 g.), $[\alpha]_D^{20}$ +107° (*c* 1·09), R_G 0·66 (neutral tank) (Found: OMe, 35·0. Calc. for $C_7H_{14}O_5$: OMe, 34·8%), which gave formaldehyde (dimedone derivative, m. p. and mixed m. p. 187—188°) in good yield on oxidation with periodate, and which after oxidation with bromine water was converted into the characteristic lactone, m. p. 36°, $[\alpha]_D^{20}$ −26° (*c* 2·44), and amide, m. p. and mixed m. p. 158—159°, of 2 : 3-di-*O*-methyl-L-arabonic acid (specimen kindly given by Dr. L. Hough).

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CHEMISTRY DEPARTMENT, UNIVERSITY OF EDINBURGH. [*Received, November 2nd,* 1956.]

[14] Hirst, Hough, and Jones, *J.*, 1949, 928.
[15] Barry and Mitchell, *J.*, 1954, 4020.

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362. *A Simplified Preparation of 4-Benzoyloxycyclohexanol.*

By D. A. V. Dendy and D. A. H. Taylor.

4-Benzoyloxy*cyclo*hexanol is useful for the synthesis of alicyclic compounds. The best recorded preparation is that of Owen and Robins as modified by Jones and Sondheimer:[1] treating quinitol with benzoyl chloride under carefully controlled conditions gives a yield of about 60%, with much quinitol dibenzoate. In our hands this has proved cumbersome and sensitive to conditions, in some runs only the dibenzoate being obtained. Since a reaction under equilibrating conditions is the most suitable for this preparation, base-catalysed ester interchanges were investigated. Heating either ethyl benzoate and quinitol, or quinitol dibenzoate and ethanol, in the presence of sodium ethoxide gave mixtures containing 50—60% of quinitol monobenzoate. Although this yield is no higher than Jones and Sondheimer's, the method is quick and simple, and quinitol and its dibenzoate are readily recovered and recycled.

Experimental.—(*a*) Quinitol (189 g.; crude *cis–trans* mixture) and ethyl benzoate (240 g.), both dried by distillation, were added to a solution of sodium (100 mg.) in ethanol (50 ml.). The solution was then heated for ½ hr. (to distil out ethanol), during which the internal temperature was raised to 250°, then acidified with acetic acid and distilled in a vacuum. After a fore-run (mainly quinitol), 4-benzoyloxy*cyclo*hexanol (210 g., 53%) was collected at 180°/0·2 mm. The residue was quinitol dibenzoate.

The ethyl benzoate may be replaced by an equivalent amount of quinitol dibenzoate.

(*b*) Quinitol dibenzoate (165 g.) was added to a solution of sodium (100 mg.) in ethanol (31 ml.) and the whole refluxed for ½ hr., neutralised with acetic acid, and distilled in a vacuum. After a fore-run (quinitol and ethyl benzoate), 4-benzoyloxy*cyclo*hexanol (56 g., 48%) was collected.

University of Liverpool. [*Received, November 9th,* 1956.]

[1] Owen and Robins, *J.*, 1949, 320; Jones and Sondheimer, *J.*, 1949, 615.

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363. *Reactivity of the Carbonyl Group in Xanthones.*

By Neil Campbell, (Miss) Sheila R. McCallum, and Donald J. Mackenzie.

The reactions of γ-pyrones, chromones, etc., with hydroxylamine are sluggish although isolated examples of formation of oxime, and *p*-nitro- and 2 : 4-dinitro-phenylhydrazone are recorded.[1] Xanthone is stated not to form an oxime, phenylhydrazone, or semicarbazone,[2] but we have prepared an oxime and a 2 : 4-dinitrophenylhydrazone, the former by heating xanthone with hydroxylamine in pyridine.[3] Xanthone could not be converted directly into the phenylhydrazone, hydrazone, or semicarbazone, but the phenylhydrazone was obtained from the oxime. The oxime and the phenylhydrazone resembled the derivatives obtained from xanthione.[4]

We have confirmed that 2-chloro-7-methylxanthone-1-carboxylic acid reacts readily with phenylhydrazine to give a pyridazone (I; R = Cl, R′ = Me).[5] 2 : 3 : 4-Trichloro-7-methylxanthone-1-carboxylic acid under the same conditions, however, gives a product believed to be the phenylhydrazono-phenylhydrazone (II). Xanthone-1-carboxylic acid itself rapidly gives a pyridazone (I; R = R′ = H).

The carbonyl reactivity of xanthone is therefore enhanced when reaction is accompanied

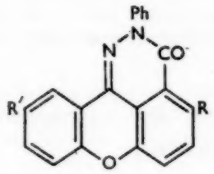
[1] Simonis and Rosenberg, *Ber.*, 1914, **47**, 1232; Bedeker *et al.*, *J. Indian Chem. Soc.*, 1935, **12**, 465; Wittig and Bangert, *Ber.*, 1925, **58**, 2636; Mozingo and Adkins, *J. Amer. Chem. Soc.*, 1938, **60**, 669; Baker, Marborne, and Ollis, *J.*, 1952, 1294.

[2] Speigler, *Ber.*, 1884, **17**, 807; Fosse, *Ann. Chim.*, 1916, **6**, 13.

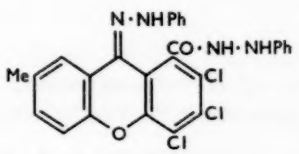
[3] Cf. Meisenheimer and Mahler, *Annalen*, 1934, **508**, 191.

[4] Graebe and Röder, *Ber.*, 1899, **32**, 1688; Mann and Turnbull, *J.*, 1951, 757.

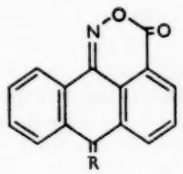
by ring-formation. In the anthraquinones also reaction with phenylhydrazine, etc., occurs readily only when a chloro-,[6] carboxyl-,[7] benzoyl-,[8] or amino-group[9] occupies the 1-position; a heterocyclic product is obtained in each case and attack occurs almost exclusively at the 9-carbonyl group. We find that merely heating (½ hr.) anthraquinone-1-carboxylic acid with phenylhydrazine and pyridine gives 2 : 3-dihydro-2-phenyl-3-oxo-1 : 2-diaza*meso*benzanthrone;[7] anthraquinone under these conditions is unchanged. The



(I)



(II)



(III)

acid is reported to react with hydroxylamine to give the oxazone (III; R = O);[7] if it is heated (4 hr.) with hydroxylamine and pyridine, the oxime (III; R = NOH) is obtained.

1-Chloro-4-methyl- and 4-chloro-1-methyl-thiaxanthone do not react with hydroxylamine in pyridine, but 2-methylthiaxanthone dioxide forms an oxime.

Experimental.—Xanthone derivatives. Xanthone (5 g.), hydroxylamine hydrochloride (25 g.), and pyridine (50 ml.) were boiled (24 hr.); pyridine (25 ml.) was then distilled off and the residue poured into water. The oxime was obtained in needles (from benzene), m. p. 161° (lit., 161°) (Found: C, 73·7; H, 4·3; N, 6·5. Calc. for $C_{13}H_9O_2N$: C, 73·9; H, 4·3; N, 6·6%). In sulphuric acid it gives a yellow solution with a blue fluorescence and when heated with hydrochloric acid yields xanthone. The oxime (1 g.) and phenylhydrazine (1 g.) were boiled (12 hr.) and then poured into water. The precipitate was washed with warm dilute hydrochloric acid and then with water, and was finally boiled in methanol. Xanthone phenylhydrazone remained as insoluble yellow needles (from acetic acid), m. p. 149—150° (lit., 152°) (Found: N, 10·1. Calc. for $C_{19}H_{14}ON_2$: N, 10·4%). The phenylhydrazone in concentrated sulphuric acid gives a dark green solution with a pale green fluorescence. Xanthone (2 g.), 2 : 4-dinitrophenylhydrazine (2 g.), concentrated sulphuric acid (4 ml.), and ethanol (30 ml.) were boiled (4 hr.). *Xanthone* 2 : 4-*dinitrophenylhydrazone* formed red crystals (from tetralin), m. p. 278° (Found: N, 15·2. $C_{19}H_{12}O_5N_4$ requires N, 14·9%).

2 : 3 : 4-Trichloro-7-methylxanthone-1-carboxylic acid (0·25 g.) and phenylhydrazine (2 ml.) were boiled (5 min.) and diluted with ethanol. The cold solution deposited the *phenylhydrazono-phenylhydrazone* (II), orange needles (from acetic acid), m. p. 316—319° (Found: C, 59·8; H, 3·0; N, 10·0; Cl, 20·0. $C_{27}H_{19}O_2N_4Cl_3$ requires C, 60·3; H, 3·5; N, 10·4; Cl, 19·7%).

Xanthone-1-carboxylic acid (0·1 g.) was boiled (5 min.) with phenylhydrazine (1 c.c.) and pyridine (5 c.c.), the mixture poured into water, and the resulting *pyridazone* crystallised from ethanol; it formed needles, m. p. 240° (decomp.) (Found: C, 76·4; H, 3·8; N, 9·1. $C_{20}H_{12}O_2N_2$ requires C, 76·9; H, 3·9; N, 9·0%). In the absence of pyridine, only nitrogen-free products were obtained.

Anthraquinone-1-carboxylic acid derivatives. Anthraquinone-1-carboxylic acid (0·5 g.), phenylhydrazine (3 c.c.), and pyridine (10 c.c.) were boiled (½ hr.) and cooled. The oxodiaza-*meso*benzanthrone crystallised from acetic acid in yellow needles, m. p. 298—299° (lit., 292°) (Found: C, 77·7; H, 3·8; N, 8·3. Calc. for $C_{21}H_{12}O_2N_2$: C, 77·8; H, 3·7; N, 8·6%).

The acid (1 g.), hydroxylamine hydrochloride (5 g.), and pyridine (25 c.c.) were boiled (4 hr.), the mixture poured into water, and the product crystallised from acetone–ethanol. The *hydroxyimino-oxazone* (III; R = NOH) separated in needles, m. p. 228—230° (decomp.) (Found: C, 68·1; H, 3·4; N, 11·0. $C_{15}H_8O_3N_2$ requires C, 68·2; H, 3·1; N, 10·6%).

[5] Knesebeck and Ullmann, *Ber.*, 1922, **55**, 306.
[6] Freund and Achenbach, *Ber.*, 1910, **43**, 3251.
[7] Ullmann and van der Schalk, *Annalen*, 1912, **388**, 212.
[8] Schaarschmidt, *Ber.*, 1915, **48**, 831; Waldmann and Oblath, *Ber.*, 1938, **71**, 366.
[9] Beilstein, "Handbuch der organischen Chemie," 1931, Vol. 14, 178.

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2-Methylthiaxanthone dioxide oxime. The dioxide (2 g.), hydroxylamine hydrochloride (10 g.), and pyridine (25 c.c.) were boiled (4 hr.) and then poured into water. The oxime crystallised from aqueous acetone in yellow needles, m. p. 199—200° (Found: C, 61·9; H, 4·3; N, 5·4; S, 11·7. $C_{14}H_{11}O_3SN$ requires C, 61·5; H, 4·1; N, 5·1; S, 11·7%).

Thanks are expressed to Dr. O. Kruber for a sample of xanthone-1-carboxylic acid, Dr. T. M. Sharp for supplying thiaxanthones, Dr. S. Coffey for samples of thiaxanthone dioxides, and the British Petroleum Oil Co. Ltd. for a grant.

THE UNIVERSITY, EDINBURGH. [*Received, November 12th*, 1956.]

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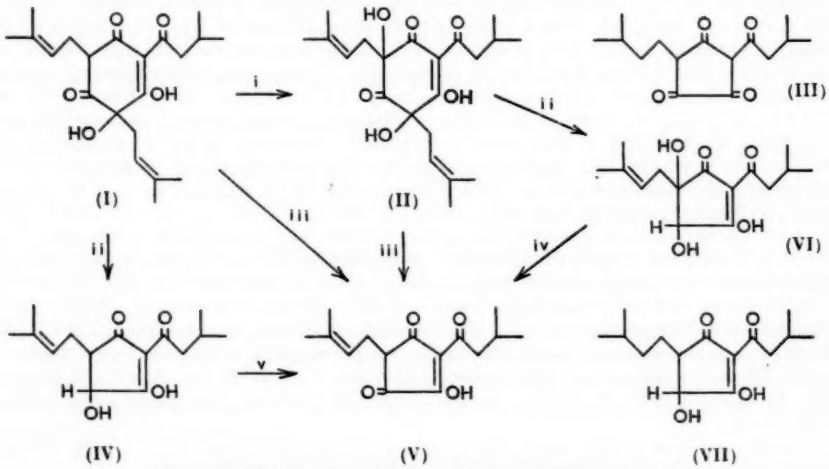
364. *The Chemistry of Hop Constituents. Part X.* Structure of a Degradation Product of Humulinone.*

By G. A. HOWARD and C. A. SLATER.

PREVIOUS work led to structure (II) being suggested [1] for humulinone, compared with the formulation (I) for its precursor, humulone. The latter is isomerised by alkali, and in particular its behaviour towards methanolic potassium hydroxide has been extensively investigated.[2,3] The effect of this reagent on humulinone was therefore studied.

A crystalline product was obtained which proved however, not to be isomeric with humulinone but had the empirical formula $C_{15}H_{20}O_4$. The compound resembled *iso*-humulinic acid (III) [4] in its yellow colour, its ultraviolet absorption spectrum, and the purple colour given with methanolic ferric chloride. It contained one double-bond and thus was possibly the enolised *cyclo*pentanetrione (V). As dihydrohumulinic acid (VII) is



i, O. ii, NaOH—H_2O. iii, KOH—MeOH. iv, $KHSO_4$. v, Bi_2O_3.

oxidised by bismuth trioxide to *iso*humulinic acid (III),[5] humulinic acid (IV) was accordingly oxidised similarly. The reaction was smooth and gave the same compound as was obtained from humulinone (m. p., reactions, and infrared spectra).

* Part IX, *J. Inst. Brewing*, 1956, 220.

[1] Cook, Howard, and Slater, *J. Inst. Brewing*, 1955, 321.
[2] Carson, *J. Amer. Chem. Soc.*, 1932, **74**, 4615.
[3] Howard, Slater, and Tatchell, *J. Inst. Brewing*, in the press.
[4] Harris, Howard, and Pollock, *J.*, 1952, 1906.
[5] Howard, Pollock, and Tatchell, *J.*, 1955, 174.

Humulinone is degraded by aqueous alkali principally to oxyhumulinic acid [1] (VI). As this compound is stable to methanolic potash, it cannot be an intermediate in the formation of the enolised trione (V) from humulinone. Nevertheless it is readily dehydrated by potassium hydrogen sulphate to the trione (V).

Humulone itself with alcoholic potassium hydroxide gives,[2,3] among other products, a compound, $C_{15}H_{20}O_4$, whose known properties leave no doubt [2] that it is the trione (V). It is suggested that its formation from humulone (I) proceeds *via* humulinone, and it is significant in this connection that Carson [2] made no attempt to exclude oxygen when he treated humulone with methanolic potash.[2]

Experimental.—Humulinone. Humulone (15·7 g.) in ether (30 ml.), underlayered with saturated aqueous sodium hydrogen carbonate (150 ml.), was oxidised with cumene hydroperoxide (10 ml.). After 5 days at room temperature the sodium salt (14·5 g.) of humulinone was filtered off; after a further 3 days an additional 1 g. separated, giving an overall yield of 89%.

Preparation of 5-(3-*methylbut*-2-*enyl*)-3-iso*valeryl*cyclo*pentane*-1 : 2 : 4-*trione from humulinone.* Humulinone (14·5 g.) was heated under reflux with methanolic potassium hydroxide (0·75 g. in 164 ml.) in nitrogen for 3 hr. The solution was cooled and poured into 2N-hydrochloric acid (200 ml.) containing crushed ice (100 g.). Extraction with light petroleum gave a syrup (5·6 g.) which partially crystallised. Crystallisation from light petroleum and then from aqueous ethanol gave the enolised cyclo*pentanetrione* as lemon-yellow prisms (0·25 g.), m. p. 136° (Found : C, 68·1, 68·0; H, 7·8, 7·8%; equiv., 264; I value, 94. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%; equiv., 264; I value for 1 double-bond, 96). Light absorption : in ethanol, $\lambda_{max.}$ 255 and 280 mμ ($E^{1\%}_{1\,cm.}$ 818 and 681); in alkaline ethanol, $\lambda_{max.}$ 275 and 303 mμ ($E^{1\%}_{1\,cm.}$ 978 and 982). This material, which gave a purple colour with methanolic ferric chloride, did not depress the m. p. of *iso*humulinic acid (m. p. 142°; I value, 0).

Evaporation of the mother-liquors yielded an intensely bitter syrup which failed to give any acyl*cyclo*pentanetrione (V) when boiled with methanolic potassium hydroxide for a further 6 hr. Neither was it possible to obtain this compound by heating oxyhumulinic acid with methanolic potassium hydroxide for 3 hr.

Preparation of the cyclo*pentanetrione* (V) *from humulinic acid.* Humulinic acid [4] (0·6 g.) was heated under reflux with bismuth trioxide (1 g.) in glacial acetic acid (25 ml.) for 5 hr. The resulting solution was poured into 2N-hydrochloric acid (50 ml.). The yellow crystals were recrystallised from aqueous ethanol (charcoal) giving a compound (0·2 g.), m. p. 135° alone or on admixture with the material described above. The infrared absorption spectrum of this compound was identical with that of the product described above.

Preparation of the cyclo*pentanetrione* (V) *from oxyhumulinic acid.* Oxyhumulinic acid [1] (0·5 g.) was mixed with finely powdered anhydrous potassium hydrogen sulphate (0·5 g.), and the mixture was gently heated. A vigorous reaction set in and the heating was stopped. The resulting orange mass was extracted with methanol (2 × 5 ml.), and the extract was treated with charcoal, filtered, and diluted with water. The crystals which separated gave, on recrystallisation from aqueous ethanol, pale yellow prisms (0·05 g.), m. p. 132—133° alone or on admixture with the acyl*cyclo*pentanetrione described above.

We are indebted to Mr. M. F. Carroll for infrared data.

BREWING INDUSTRY RESEARCH FOUNDATION,
NUTFIELD, SURREY.

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XUM

365. *Preparation of the Di-*p*-toluoyl Derivative of (−)-Tartaric Acid.*

By J. H. Hunt.

Stoll and Hofmann [1] have described the preparation of both optical antipodes of di-*p*-toluoyltartaric acid, which are useful resolving agents, by the acylation of (+)- and (−)-tartaric acid with *p*-toluoyl chloride. When the (−)-isomer is required, this method suffers from the disadvantage that the isolation in good yield of (−)-tartaric acid by resolution of racemic acid with cinchonine [2] is somewhat tiresome because the acid is water-soluble and isolation through the lead salt is necessary.

It has now been found that (±)-di-*p*-toluoyltartaric acid is readily resolved by cinchonine, giving a good yield of the cinchonine salt of the (−)-acid from which the free diacylated acid can easily be obtained having an optical rotation identical with that recorded previously.[1]

Some samples prepared by both methods have shown evidence of polymorphism, melting at 148°, resolidifying, and finally melting at 168° (uncorr.) [Stoll and Hofmann [1] give 172° (corr.)]. This is especially apparent in these samples on rapid heating. After recovery of cinchonine, the residue from the mother-liquors may be worked up to give a smaller yield of the (+)-isomer or can conveniently be hydrolysed to recover *p*-toluic acid.

Experimental.—(±)-OO-*Di*-p-*toluoyltartaric anhydride* was prepared from racemic acid (35·6 g.) [3] and *p*-toluoyl chloride (117 g.) by Stoll and Hofmann's method.[1] Recrystallised from xylene, it had m. p. 162—163° (Found: C, 64·8; H, 4·45. $C_{20}H_{16}O_7$ requires C, 65·2; H, 4·4%).

(±)-OO-*Di*-p-*toluoyltartaric acid.* The anhydride (32 g.) was refluxed for 2 hr. with acetone (75 ml.) and water (7·5 ml.), and the mixture evaporated. The solid residue was boiled with xylene to remove unchanged anhydride and filtered hot. The air-dried insoluble *product* (25 g.) had m. p. 183—184° and was sufficiently pure for the next stage. A sample recrystallised from nitrobenzene had m. p. 188° (Found: C, 62·2; H, 4·6. $C_{20}H_{18}O_8$ requires C, 62·3; H, 4·7%).

Resolution. The racemic acid (25 g.) was added to a suspension of cinchonine (19 g.) in boiling alcohol (500 ml.). The components dissolved completely and the solution on cooling deposited crystals which after 1 hr. were filtered off. The crude salt was refluxed with alcohol (60 ml.) for 15 min., filtered off, and dried at 100°. The *cinchonine* (−)-OO-*di*-p-*toluoyltartrate* so obtained (20 g.) melted at 201° and could be used without further purification. It recrystallised when treated in dimethylformamide with an equal volume of alcohol; it then melted at 208°, $[\alpha]_D^{26}$ +79·4° (*c* 0·4 in dimethylformamide) (Found: C, 68·3; H, 5·9; N, 4·2. $C_{39}H_{40}O_9N_2$ requires C, 68·8; H, 5·9; N, 4·1%).

(−)-OO-*Di*-p-*toluoyltartaric acid.* The cinchonine salt (156 g.) was suspended in water (1 l.), ether (200 ml.) added, and the whole stirred while concentrated hydrochloric acid (75 ml.) was added. The ether was separated, the mixture was extracted with a further portion of ether (200 ml.), and the combined extracts were dried ($MgSO_4$). Evaporation gave a gum which was refluxed for 1 hr. with benzene (600 ml.), during which a few crystals of the racemic compound were added to induce crystallisation of any traces remaining. The solution was filtered hot and allowed to cool slowly. Next morning the acid was filtered off, washed with benzene, and dried at 60° (81 g.). It had m. p. 148°, resolidified, and remelted 168°; $[\alpha]_D^{20}$ +138° (*c* 1 in alcohol). After recrystallisation from benzene the m. p. was unchanged, and $[\alpha]_D^{25}$ was +140° (Found: C, 62·3; H, 4·7%). Stoll and Hofmann [1] report m. p. 172° (corr.), $[\alpha]_D$ +140°.

The pure acid is slowly soluble in about 70 parts of boiling benzene. Its solubility is, however, greatly increased by the addition of small amounts of acetone or ether and in the

[1] Stoll and Hofmann, *Helv. Chim. Acta*, 1943, **26**, 922.
[2] Marckwald, *Ber.*, 1896, **29**, 42.
[3] Church and Blumberg, *Ind. Eng. Chem.*, 1951, **43**, 1780.

above procedure, the gummy product retains sufficient ether for complete solution in the quantity of benzene stated.

The author thanks Miss P. Schaay for technical assistance and the Directors of Allen & Hanburys Ltd. for permission to publish these results.

RESEARCH DIVISION, ALLEN & HANBURYS LTD.,
WARE, HERTS.

[*Received, November 13th,* 1956.]

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366. *The Reduction of Ruthenium Tetroxide in Hydrofluoric Acid.*

By M. L. HAIR, M. A. HEPWORTH, and P. L. ROBINSON.

RUFF [1] found that aqueous hydrofluoric acid, in contrast to the other halogen acids, is without action on ruthenium tetroxide. The tetroxide can be reduced electrolytically [2] in perchloric acid to give a solution containing Ru^{IV} and Ru^{III}, these valency states being characterised by their absorption spectra. A Ru^{IV} solution in nitric acid [3] was obtained from the reaction between ruthenium tetroxide and hydrogen peroxide in the aqueous acid. The use of hydrogen peroxide as a reducing agent has now been extended to solutions in aqueous hydrofluoric acid.

Solutions of Ru^{IV} in nitric acid contain [3] the cationic species $[Ru(H_2O)_5OH]^{3+}$ and it is probable that a similar ion is present in perchloric acid solutions. In common with perchlorate and nitrate, the fluoride ion is a poor complexing ligand for noble metals compared with chloride, cyanide, or nitrite. This gives grounds for expecting it to be present in the corresponding solutions of Ru^{IV} in hydrofluoric acid, as has now been realised, for their evaporation at room temperature permits the isolation of solid $[Ru(H_2O)_5OH]F_3$ which, however, is largely decomposed with loss of hydrogen fluoride and water when heated to 100°. The corresponding nitrate has previously been isolated.[3] The deep colour of solutions with the ruthenium in the cation is in marked contrast with those containing the $[RuF_6]^{2-}$ anion,[5] which are almost colourless.

Experimental.—Ruthenium metal sponge was converted into the tetroxide by Martin's [4] method. The tetroxide (0·5 g.) was washed into a platinum dish, suspended in "AnalaR" 40% hydrofluoric acid (15 ml.) and treated, dropwise, with pure 30% hydrogen peroxide solution. Oxygen was copiously evolved and the tetroxide dissolved to a deep red solution; when the reaction was complete the temperature was raised on a steam-bath to 100° to decompose excess of hydrogen peroxide.

After dilution, the absorption spectrum of the solution was measured in a Unicam ultra-violet spectrophotometer with 1 cm. matched Perspex cells. This was identical with that found for a Ru^{IV} solution in perchloric acid.[3] That the ruthenium was present in the cation was shown by the solution's losing its colour by exchange with hydrogen ion when passed through a Polythene column containing Zeo-Karb 225 resin in the hydrogen form.

Evaporation of the Ru^{IV} solution in a vacuum desiccator (KOH) left a vitreous, black solid {Found: Ru, 39·9; F, 21·1. $[Ru(H_2O)_5OH]F_3$ requires Ru, 38·3; F, 21·5%}. This solid dissolves readily in water to re-form the original red solution. When evaporated to dryness on a steam-bath it left a black solid which was virtually insoluble in both water and hydrofluoric acid (Found: Ru, 47·3; F, 11·4%). These evaporations must be carried out as soon as possible. On allowing the original solution to stand overnight further reduction takes place and spectroscopic evidence shows the presence of the hydrated Ru^{III} ion.

Acknowledgment is made of a British Titan Product Fellowship (M. A. H.) and a maintenance grant from the Department of Scientific and Industrial Research (M. L. H.).

KING'S COLLEGE, NEWCASTLE UPON TYNE, 1.

[*Received, November 14th,* 1956].

[1] Ruff and Vidic, *Z. anorg. Chem.*, 1924, **136**, 52.
[2] Wehner and Hindman, *J. Amer. Chem. Soc.*, 1950, **72**, 3911.
[3] Fletcher, Jenkins, Lever, Martin, Powell, and Todd, *J. Inorg. Nuclear Chem.*, 1955, **1**, 378.
[4] Martin, *J.*, 1952, 3055.
[5] Hepworth, Peacock, and Robinson, *J.*, 1954, 1197.

XUM

367. 3-*Methyl*-3-*phenyloxindole.*

By (Miss) E. F. M. Stephenson.

3-Methyl-3-phenyloxindole has been prepared in good yield by cyclisation of (±)-atrolactanilide with polyphosphoric acid. With the same reagent (±)-mandelanilide gave 3-phenyloxindole.[1] (±)-Atrolactanilide was obtained from methyl (±)-atrolactate by Bodroux's method.[2]

Experimental.—M. p.s marked * were determined on a Kofler hot-stage microapparatus. Microanalyses were made by the C.S.I.R.O. Microanalytical Service. Temperatures quoted for sublimations refer to the heating-bath. The phosphoric acid had *d* 1·75.

Methyl (±)-*atrolactate.* A mixture of anhydrous (±)-atrolactic acid (33·2 g.), absolute methanol (120 ml.), and concentrated sulphuric acid (6 ml.) was refluxed for 6 hr. and methanol (85 ml.) then removed by distillation. The residue was poured into ice-water and extracted with benzene, the benzene distilled off, and the *ester* distilled under reduced pressure; it had b. p. 83—85°/1·3 mm., n_D^{20} 1·5154 (Found: C, 66·9; H, 6·8. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

(±)-*Atrolactanilide.* A solution of ethylmagnesium bromide [from magnesium (1·31 g.), ethyl bromide (4·5 ml.), and ether (40 ml.)] was cooled in ice, and aniline (5·15 ml.) in ether (10 ml.) added with shaking during 8—10 min. The mixture was kept for 0·5 hr. at room temperature, then again cooled in ice, methyl (±)-atrolactate (2·7 g.) in ether (30 ml.) was added with shaking during 3 min., and the mixture refluxed for 0·5 hr. and decomposed with ice and dilute sulphuric acid. The ether layer gave an oil which was freed from aniline by being stirred with dilute sulphuric acid. The *anilide* (2·28 g.) formed plates, m. p.* 136·5—137·5°, from aqueous ethanol (Found: C, 74·4; H, 6·4; H, 5·7. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·3; N, 5·8%).

3-*Methyl*-3-*phenyloxindole.* To a solution of phosphoric oxide (5·3 g.) in phosphoric acid (3 ml.) at 107° (±)-atrolactanilide (0·3 g.) was added rapidly, and the internal temperatures of the stirred mixture was raised from 110° to 116° during 55 min. The hot solution was poured on ice and after several hours crystallisation of the product was complete. After sublimation at 160°/0·7 mm. and crystallisation from aqueous ethanol, the *oxindole* (215 mg.) formed prisms, m. p.* 155—156 (Found: C, 80·8; H, 5·9; N, 6·3; O, 7·5. $C_{15}H_{13}ON$ requires C, 80·7; H, 5·9; N, 6·3; O, 7·2%). Attempts to cyclise atrolactanilide with sulphuric acid did not give useful results. 3-Methyl-3-phenyloxindole dissolves rapidly in warm dilute aqueous sodium hydroxide and is reprecipitated on acidification.

3-*Phenyloxindole.* To a solution of phosphoric oxide (5·3 g.) in phosphoric acid (3 ml.) at 106° (±)-mandelanilide (0·23 g.) was added rapidly, and the internal temperature of the stirred mixture was raised from 106° to 120° in 95 min. As the anilide dissolved the solution became rose-pink but the colour faded as cyclisation proceeded. The hot, pale brown solution was poured on ice and after 2 hr. crystallisation of the product was complete. After sublimation at 155°/0·3 mm. and crystallisation from aqueous ethanol, the oxindole (80 mg.) had m. p.* 184—185° (Found: C, 80·4; H, 5·3; N, 6·7. Calc. for $C_{14}H_{11}ON$: C, 80·4; H, 5·3; N, 6·7%). 3-Phenyloxindole has been prepared by Meisenheimer and Meis and by Palazzo and Rosnati [1] in unspecified yield by cyclisation of (±)-mandelanilide with concentrated sulphuric acid.

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Chemistry Department, University of Melbourne,
Carlton, N.3, Victoria, Australia. [*Received, November 19th,* 1956.]

[1] Meisenheimer and Meis, *Ber.*, 1924, **57**, 297; Palazzo and Rosnati, *Gazzetta*, 1953, **83**, 211.
[2] Bodroux, *Compt. rend.*, 1904, **138**, 1427; 1906, **142**, 401; *Bull. Soc. chim. France*, 1905, **33**, 832; cf. Hardy, *J.*, 1936, 398.

368. *The Synthesis of* (±)-*Felinine.*

By S. Trippett.

Westall [1] isolated from cat's urine a non-crystalline sulphur-containing amino-acid, felinine, which gave no crystalline derivatives and was optically active. Desulphurisation with Raney nickel gave alanine and *iso*pentyl alcohol, and on this basis Westall suggested structure (I) for felinine. The racemic compound (I) has now been synthesised and shown to be (±)-felinine.

$HO{\cdot}CH_2{\cdot}CH_2{\cdot}CMe_2{\cdot}S{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CO_2H$ (I)

$HO_2C{\cdot}CH(NH_2){\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CH_2{\cdot}CMe_2{\cdot}S{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CO_2H$ (II)

The addition of toluene-ω-thiol to β-methylcrotonaldehyde gave β-(benzylthio)*iso*valeraldehyde [2] which, on reduction with lithium aluminium hydride, gave 2-(benzylthio)-*iso*pentyl alcohol. Treatment of this with sodium in liquid ammonia gave the sodium salt of the thiol which was coupled *in situ* with α-amino-β-chloropropionic acid to give in good yield *S*-(3-hydroxy-1 : 1-dimethylpropyl)cysteine (I).

This was shown to be (±)-felinine by the following evidence. (i) The synthetic material behaved on paper chromatography exactly as did natural (−)-felinine in the five solvent systems examined. (ii) Oxidation with hydrogen peroxide at the origin of a paper chromatogram led to the disappearance of the original spot and to the appearance of a new spot in the same position as that from a similar oxidation of natural felinine. (iii) Treatment of the synthetic material with 5N-hydrochloric acid at 105° gave a mixture of unchanged amino-acid and of free cystine together with a new amino-acid, $C_{11}H_{22}O_4N_2S_2$ [probably (II)], which ran on paper in the alanine region; natural felinine behaved in exactly the same way.[1] (iv) Final proof was obtained by the preparation from the synthetic racemate of a crystalline *N*-2 : 4-dinitrophenyl derivative which had the same infrared spectrum as the non-crystalline *N*-2 : 4-dinitrophenyl derivative prepared from natural (−)-felinine and purified by chromatography.

Experimental.—2-(*Benzylthio*)iso*pentyl alcohol.* A solution of β-(benzylthio)*iso*valeraldehyde (10 g.) in ether (100 ml.) was added slowly to a solution of lithium aluminium hydride (0·7 g.) in ether (50 ml.), and the resulting suspension was refluxed for 15 min., cooled in ice, and decomposed by dilute sulphuric acid. Ether extraction gave 2-(*benzylthio*)iso*pentyl alcohol*, b. p. 120—122°/0·3 mm. (Found : C, 68·3; H, 8·8. $C_{12}H_{18}OS$ requires C, 68·5; H, 8·6%).

(±)-*Felinine.* To a stirred solution of 2-(benzylthio)*iso*pentyl alcohol (1·05 g.) in liquid ammonia (100 ml.), sodium was added in small pieces until a permanent blue colour was obtained. α-Amino-β-chloropropionic acid (0·46 g.) was then added and the ammonia allowed to evaporate. The residue was taken up in water (50 ml.) and placed on a column of Dowex 50 (acid form; 2 × 10 cm.) which was then washed with water till the eluate was neutral. The amino-acid was then eluted with 0·5N-ammonia. Evaporation of the eluate and crystallisation from aqueous ethanol gave S-(3-*hydroxy*-1 : 1-*dimethylpropyl*)*cysteine*, m. p. 181° (decomp.) (Found : C, 45·9; H, 8·1; N, 6·7. $C_8H_{17}O_3NS$ requires C, 46·4; H, 8·2; N, 6·8%). This material ran on paper exactly as did a sample of natural (−)-felinine in the following solvent systems, the approximate R_f values being given in parentheses : butan-1-ol–acetic acid–water (5 : 1 : 4) (0·4), butan-1-ol–ethanol–water (7 : 2 : 3) (0·38), *tert.*-amyl alcohol (0·28), collidine (0·46), and phenol (0·88).

Treatment with 2 : 4-dinitrofluorobenzene gave the N-2 : 4-*dinitrophenyl derivative*, m. p. (from aqueous ethanol) 120—122° (Found : C, 45·1; H, 5·4; N, 11·6. $C_{14}H_{19}O_7N_3S$ requires C, 45·0; H, 5·1; N, 11·3%). The infrared spectrum of a solution in acetonitrile–chloroform (2 : 5 v/v), showed the expected features and was identical with that of the amorphous N-2 : 4-*dinitrophenyl derivative* of (−)-felinine, purified by chromatography in ethyl acetate on Hyflo Supercel (Found : N, 11·35%), taken in the same solvent mixture.

[1] Westall, *Biochem. J.*, 1953, **55**, 244.
[2] Catch, Cook, Graham, and Heilbron, *J.*, 1947, 1609.

XUM

Action of 5N-*hydrochloric acid on* (±)-*felinine.* (±)-Felinine (0·2 g.) was heated with 5N-hydrochloric acid (4 ml.) in a sealed tube under nitrogen for 36 hr. A small quantity of a brown oil separated and was removed. The solution was evaporated under reduced pressure and the residue, in water (20 ml.), placed on a column of Dowex 50 (acid form; 1 × 15 cm.) which was then washed with water. Elution with 0·5N-ammonia gave an amino-acid fraction which was evaporated to 3 ml. and set aside at 0° overnight. Filtration gave a *product*, m. p. 244—245° (decomp.) (Found: C, 42·2; H, 7·0; N, 8·6. $C_{11}H_{22}O_4N_2S_2$ requires C, 42·5; H, 7·1; N, 9·0%).

I thank Dr. R. G. Westall for a supply of natural felinine and Dr. J. Holgate for arranging a supply of cat's urine.

THE UNIVERSITY, LEEDS, 2. [*Received, November 19th,* 1956.]

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369. *Activity Coefficients and Transport Numbers for Hydrochloric Acid at 0°.*

By A. K. COVINGTON and J. E. PRUE.

RECENTLY it was shown [1] that an analysis of the freezing-point data [2] for hydrochloric acid gives values for the activity coefficient which differ by more than the apparent experimental accuracies from the values obtained from e.m.f. measurements.[3] In connection with other work [4,5] we have obtained values of the activity coefficient at 0° by combining e.m.f. measurements on cells with transport-number data.

Experimental.—The e.m.f. measurements were made with silver–silver chloride electrodes and the transport numbers t^+ obtained by the moving-boundary technique.[4,5] The temperature of the thermostat, which contained a 20% alcohol–water mixture, was adjusted to 0·00° ± 0·01° by comparison with the temperature of crushed ice made from distilled water and maintained with the aid of a commercial refrigerator unit.

Results.—The results are shown in Tables 1 and 2. The value adopted for the e.m.f. constant (RT/F) ln 10 was $(2{\cdot}27115 \times 10^3)(2{\cdot}30259 \times 10^3)/(0{\cdot}964877 \times 10^5) = 54{\cdot}199$ mv,

TABLE 1.

c (mole l.$^{-1}$)	$c^{\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ l.$^{-\frac{1}{2}}$)	t^+_{obs}	Vol. corr.	$t^+_{corr.}$
$0{\cdot}02151_1$	0·1468	0·8491	0·0002	0·8493
$0{\cdot}03970_2$	0·1993	0·8501	0·0004	0·8505
$0{\cdot}05787_9$	0·2404	0·8511	0·0006	0·8517
$0{\cdot}07995_9$	0·2828	0·8524	0·0007	0·8531
$0{\cdot}09739_7$	0·3121	0·8527	0·0009	0·8536
0·09928	0·3151	0·8529	0·0009	0·8538

TABLE 2.

$m_1 = 0{\cdot}10930$ mole kg.$^{-1}$ $t_1 = 0{\cdot}8538$

$10^3 m_2$ (mole kg.$^{-1}$)	E (mv)	t^+	$-\Delta \log \gamma$	$\Delta \log \gamma - \Delta \log \gamma^{at}$	Δm (mole kg.$^{-1}$)
5·825	111·59	0·8466	0·06186	0·02479	0·1035
11·35	86·02	0·8478	0·05064	0·02362	0·09795
21·25	62·16	0·8491	0·03768	0·02098	0·08805
30·25	48·73	0·8500	0·03001	0·01894	0·07905
44·34	34·26	0·8510	0·02101	0·01536	0·06496
72·55	5·62	0·8526	0·00908	0·00862	0·03675

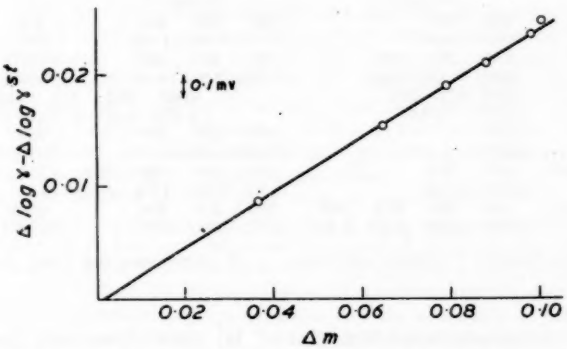
[1] Guggenheim and Prue, "Physicochemical Calculations," North-Holland Publ. Co., Amsterdam, 1955, p. 226.
[2] Randall and Vanselow, *J. Amer. Chem. Soc.*, 1924, **46**, 2418.
[3] Harned and Ehlers, *J. Amer. Chem. Soc.*, 1932, **54**, 1350.
[4] Covington and Prue, *J.*, 1955, 3701.
[5] Covington and Prue, *J.*, 1957, 1567.

for the Debye–Hückel constant (A) 0·488 (mole^{-1} kg.)$^{\frac{1}{2}}$, and for the faraday 96·488 c mole^{-1}. The volume corrections were estimated from partial molal volumes calculated from density data in the International Critical Tables.

The plot of $\Delta \log \gamma - \Delta \log \gamma^{st}$ against Δm (m = molality) gives an excellent straight line (Figure), the slope of which corresponds to

$$\log \gamma = -Am^{\frac{1}{2}}/(1 + m^{\frac{1}{2}}) + 0{\cdot}240m \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The value of the coefficient of the linear term (0·240) is in excellent agreement with that obtained from e.m.f. measurements (0·241) rather than from the freezing-point measurements (0·216). The discrepancy corresponds to a difference of slightly more than $\frac{1}{2}$% in γ at a molality of 0·1. The freezing-point measurements were analysed [1] by using the value $\lambda = 1{\cdot}860$ deg. mole^{-1} kg. for the cryoscopic constant of water based on the best modern measurements. If the older value $\lambda = 1{\cdot}858$ deg. mole^{-1} kg. had been used the discrepancy in γ at 0·1m would be reduced to about 0·3%.



Transport numbers and activity coefficients at rounded concentrations are given in Table 3. The transport numbers were smoothed by use of Shedlovsky's equation [6] modified by replacing the term $c^{\frac{1}{2}}$ by $c^{\frac{1}{2}}/(1 + c^{\frac{1}{2}})$; this in general we find gives linear plots with a smaller slope than does the original equation. In using this equation the

TABLE 3.

c	0	0·01	0·02	0·05	0·10
t^+	0·8441	0·8476	0·8490	0·8514	0·8538
m	—	0·01	0·02	0·05	0·10
γ	—	0·9079	0·8798	0·8372	0·8068

value of the equivalent conductivity at infinite dilution, Λ_0(HCl) = 265·2 int. ohm^{-1} mole^{-1} cm.^{2}, was taken from Randall and Vanselow's paper. The activity coefficient values were obtained from eqn. 1.

We are grateful to the Department of Scientific and Industrial Research for a grant to one of us (A. K. C.).

READING UNIVERSITY. [*Received, November 20th*, 1956.]

[6] Shedlovsky, *J. Chem. Phys.*, 1938, **6**, 845.

370. *Ultraviolet Absorption Spectra of Some Condensed Thiophen Derivatives.*

By W. Carruthers and J. R. Crowder.

The ultraviolet absorption spectra of polycyclic compounds derived from five-membered heterocyclic systems have recently been described by Badger and Christie,[1] who concluded that there is a fundamental similarity between the spectra of the heterocyclic compounds and those of the related benzenoid hydrocarbons. In the Table we record the spectra of some other condensed thiophen derivatives which support this conclusion.

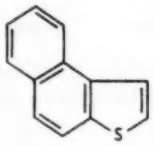
Ultraviolet absorption maxima (mμ) *with* log ε *in parentheses.**

Compound	Group I	Group II	Group III
4 : 5-Benzothio-naphthen †	245 (4·70) 255 (4·44)	281 (3·95) 292 (4·10) 304 (4·06)	316 (329) {323} {(2·88)} 330·5 (3·22)
6 : 7-Benzothio-naphthen	255 (4·55) 261 (4·68) 264 (4·66)	281 (3·92) 292 (3·84) 304 (3·53)	{317} {(2·66)} 325 (2·84) 334 (2·60) 341 (2·80)
Thiophanthren	232 (4·51) 251—255 (4·84)	{300} {(3·37)} 313 (3·61)	328 (3·72) 336 (3·76) 352 (3·84)
Thiophanthren dioxide	257 (4·79)	278 (4·03) 288 (4·01) 299 (3·99)	333 (3·16) 348 (3·41) 364 (3·46)
2-Methyl-5 : 6-benzo-thiophanthren	277 (4·74) 285 (4·60)	302 (3·88) 309 (3·92) 320 (4·04) 336 (4·10)	350 (3·20) {360} {(2·64)} 368 (2·64)
2-Methyl-7 : 8-benzo-thiophanthren	246 (4·26) 265 (4·23) 274 (4·54) 285 (4·68)	303 (4·02) 315 (4·00) 330 (3·90)	{345} {(2·88)} 353 (3·10) 362 (2·73) 372 (2·94)

* Figures with braces { } indicate inflexions. † Cf. Campaigne and Cline, *J. Org. Chem.*, 1956, **21**, 39.

4 : 5- and 6 : 7-Benzothionaphthen (I and II) show three well defined groups of absorption bands, and the similarity with the spectrum of phenanthrene is even closer than was observed in the case of dibenzothiophen.[1] Displacement of the maxima to shorter wavelengths is much less pronounced than in dibenzothiophen. The increased intensity of the long-wavelength absorption, noted by Badger and Christie, is again evident.

A similar relation is found with thiophanthren (III) whose spectrum is very similar to that of anthracene. Like the hydrocarbon it shows only two regions of absorption, but



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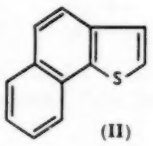

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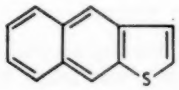


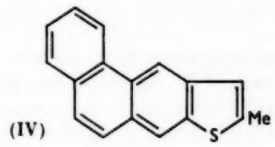
(III)

the long-wavelength maxima are displaced 20—25 mμ towards the violet, and the short-wavelength maxima are of somewhat lower intensity than in anthracene. The spectrum of the dioxide is more complicated and shows three groups of bands indicating a contribution of the SO_2 group to the conjugation. The similarity in the spectra of anthracene and thiophanthren suggests some correspondence in chemical properties, and this is being investigated.

In the tetracyclic series, the spectra of 2-methyl-5 : 6-benzothiophanthren (IV) and

[1] Badger and Christie, *J.*, 1956, 3438.

2-methyl-7 : 8-benzothiophanthren (V) are again very similar to those of their hydrocarbon analogues 7- and 6-methyl-1 : 2-benzanthracene.[2] The Group II and Group III



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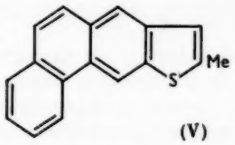

(V)

bands occur at shorter wavelengths, but the increased intensity of the Group III maxima, noted in other cases,[1] is not observed with these compounds.

Experimental.—Absorption spectra. These were determined with a "Unicam" spectrophotometer with *cyclo*hexane solutions, except in the case of thiophanthren dioxide where the solvent was 95% ethanol.

Materials. 4 : 5- and 6 : 7-Benzothionaphthen were obtained as described previously.[3]

2-Methyl-5 : 6- and 2-methyl-7 : 8-benzothiophanthren were prepared by the method of Buu-Hoï and Nguyen-Hoan.[4] The m. p. of the latter compound was found to be 112—114°, not 189° as reported by them (Found : C, 82·5; H, 4·8. Calc. for $C_{17}H_{12}S$: C, 82·2; H, 4·8%). The *picrate* formed orange-red needles, m. p. 155°, from benzene–ethanol (Found : C, 57·7; H, 3·3; N, 9·0. $C_{17}H_{12}S,C_6H_3O_7N_3$ requires C, 57·9; H, 3·2; N, 8·8%). Desulphurisation of the compound with Raney nickel in boiling ethanol [5] gave 2-*n*-propylphenanthrene as plates, m. p. 35—36° alone or mixed with an authentic specimen.

Thiophanthren was obtained in very poor yield by reduction of thiophanthraquinone [6] by boiling a suspension (2 g.) for 2 days with zinc dust (7 g.) in concentrated aqueous ammonia (25 c.c.), further portions of zinc and ammonia being added at intervals. The mixture was filtered hot, and the residue washed with water and with alkaline sodium dithionite to remove excess of quinone. The product was extracted from the insoluble portion with boiling benzene. After purification by chromatography on alumina and by sublimation, thiophanthren was obtained as colourless plates (20 mg.), m. p. 186—189°, from benzene–ethanol (lit.,[7] 189°) (Found : C, 78·4; H, 4·3. Calc. for $C_{12}H_8S$: C, 78·2; H, 4·4%). The *dioxide*, obtained when thiophanthren (10 mg.) and hydrogen peroxide (0·05 c.c., 30%) in acetic acid (1 c.c.) were heated on the water-bath for 2 hr., formed straw-coloured prisms, m. p. 177—179° (Kofler block), from benzene–methanol (Found : C, 66·5; H, 3·9. $C_{12}H_8O_2S$ requires C, 66·7; H, 3·7%).

Microanalyses were by Mr. J. M. L. Cameron and Miss M. Christie. One of us (W. C.) was supported by the Medical Research Council.

UNIVERSITY OF GLASGOW. [*Received, November 21st*, 1956.]

[2] Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, 1951, Spectra nos. 505 and 506.
[3] Carruthers, *J.*, 1953, 4186.
[4] Buu-Hoï and Nguyen-Hoan, *Rec. Trav. chim.*, 1948, **67**, 309.
[5] Blicke and Sheets, *J. Amer. Chem. Soc.*, 1948, **70**, 3768.
[6] Etienne, *Bull. Soc. chim. France*, 1947, 634.
[7] von Meyer, *Annalen*, 1931, **488**, 259.

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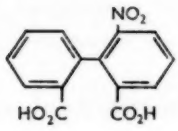
371. *A Redetermination of the Racemisation Velocities of 6-Nitro-, 4 : 6′-Dinitro-, and 4 : 6 : 4′-Trinitro-diphenic Acid in Alkaline Solution.*

By Jean W. Brooks, Margaret M. Harris, and K. E. Howlett.

The mode of operation of the nitro-group in influencing the optical stability of substituted diphenic acids is at present a matter of speculation.[1,2,3] Attempts to explain the effect of substituting further nitro-groups in the 4- and 4′-position in 6-nitrodiphenic acid (I) have so far been based upon the experimental work of Kuhn and Albrecht;[4] these authors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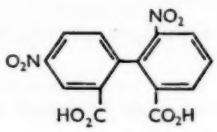
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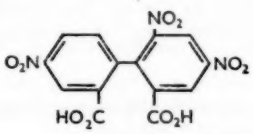
(III)

were the first to show that the decrease in optical activity of diphenyls obeys the first-order kinetic law. Their results are given in Table 1, together with the enthalpies ($\Delta H^{\ddagger}$)

Table 1.

Acid	$\frac{1}{2{\cdot}303}k$ (min.$^{-1}$) in 2N-Na_2CO_3 [4]	E (kcal. mole^{-1}) [4]	$\Delta H^{\ddagger}$ [1]	$\Delta S^{\ddagger}$ [1]
(II)	0·018 at 98·2°; 0·0014 at 73·5°	26	25·7	−4·2
(III)	0·0060 at 98·6°; 0·00074 at 74·6°	22·4	21·2	−18·5

and entropies ($\Delta S^{\ddagger}$) of activation calculated by Cagle and Eyring [1] using Kuhn and Albrecht's data.

The racemisation of 6-nitrodiphenic acid (I) in 0·1N-sodium hydroxide was investigated by Adams and Hale [5] at one temperature only, presumably the boiling point of the solution. A half-life of 4·6 minutes was recorded.

We have now repeated the observation of the racemisation of these acids, in greater detail, in 2N-sodium carbonate (not sodium hydroxide [1,5]) solution. Table 2 shows the

Table 2.

Acid	Temp.	10^4k (sec.$^{-1}$)	E (kcal. mole^{-1})	A (sec.$^{-1}$)	$\Delta S^{\ddagger}$ (e.u.)
(I)	87·6°	8·05	22·6	$10^{10\cdot6}$	−12·2
	80·6	4·24			
	67·55	1·26			
	57·0	0·435			
(II)	91·0	3·42	22·6	$10^{10\cdot1}$	−14·7
	83·4	1·69			
	74·4	0·769			
	70·4	0·515			
(III)	94·0	1·90	22·6	$10^{9\cdot7}$	−16·3
	84·6	0·85			
	82·0	0·66			
	72·4	0·275			

first-order racemisation velocity constants and the parameters for the corresponding rate equations.

[1] Cagle and Eyring, *J. Amer. Chem. Soc.*, 1951, **73**, 5628.
[2] de la Mare, "Progress in Stereochemistry," Ed. Klyne, Butterworths, London, Vol. I, 1954, p. 120.
[3] Westheimer, "Steric Effects in Organic Chemistry," Ed. Newman, John Wiley, New York, 1956, p. 553.
[4] Kuhn and Albrecht, *Annalen*, 1927, **455**, 272; **458**, 221.
[5] Adams and Hale, *J. Amer. Chem. Soc.*, 1939, **61**, 2825.

In calculating $\Delta S^{\ddagger}$ from the formula $k = \kappa e \frac{kT}{h} \exp(\Delta S^{\ddagger}/R - E/RT)$ the value of the transmission coefficient κ is taken as unity in each case.

The marked increase in optical stability on addition of a further nitro-group in a *para*-position (where it can exercise neither a blocking nor a buttressing effect) is here shown to reside in the entropy-of-activation factor rather than in the activation energy of the racemisation process.

The authors are indebted to the Department of Scientific and Industrial Research for a maintenance grant (to J. W. B.).

BEDFORD COLLEGE, LONDON, N.W.1. [*Received, December 6th,* 1956.]

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372. *The Interaction of Phenacyl Chloride and Aqueous Alkali.*

By C. EABORN.

THE reaction between phenacyl halides and alcoholic alkalis has been much studied,[1] and high yields of "α- and β-diphenacyl halides" (2-benzoyl-3-halogenomethyl-3-phenyloxirans) have been obtained. Thus phenacyl chloride with potassium hydroxide in methanol gives the "diphenacyl chlorides" in 95% yield,[2] and phenacyl bromide with sodium ethoxide in ethanol gives "diphenacyl bromide" in 83% yield.[1] There appear to be no reports, however, of the interaction of phenacyl halides and aqueous alkali, and when we examined this we were surprised to obtain mandelic acid in *ca.* 45% yield. When as little as 30% of methanol was added to the aqueous system mandelic acid was no longer formed. At first sight the acid might seem to result from an unusual rearrangement, but since we find that phenacyl alcohol, which is known to be readily oxidized,[3] is converted into mandelic acid under the reaction conditions we believe that this alcohol is first formed and is then oxidized, presumably by atmospheric oxygen. In agreement with this suggestion, much less mandelic acid was obtained when the reaction was carried out in a nitrogen atmosphere, and the small quantity obtained was probably formed during the working-up. Probably the very low solubility of phenacyl chloride in water reduces the chance of the self-condensation to give the "diphenacyl chlorides," and simple substitution at the C–Cl bond is allowed to proceed.

Experimental.—Phenacyl chloride and aqueous alkali. Phenacyl chloride (5 g.) was added in small portions during 1 hr. to a stirred solution of sodium hydroxide (10 g.) in water (100 ml.) kept at 65—70°, and the mixture was stirred at this temperature for ½ hr. longer. The orange solution was cooled and decanted from a red solid (2·2 g., after drying) and then extracted with ether, the extract being discarded. Acidification of the solution followed by extraction with large volumes of ether and removal of the solvent from the extracts gave (±)-mandelic acid (2·1 g., 43%), m. p. and mixed m. p. 118—120° after recrystallization from ether–light petroleum. The m. p. was depressed on admixture with benzoic acid.

When the reaction was carried out under nitrogen, but with exposure of the system to the air during extraction processes, only 0·3 g. of mandelic acid was obtained. Acidification of the alkaline solution [after decantation from the red solid (2·5 g.) and extraction with ether] liberated a yellow oil which was taken up in a little ether before the mandelic acid was extracted with large volumes of ether. The oil (1·6 g.) was recovered and found to contain no material readily soluble in water.

Phenacyl chloride and aqueous methanolic alkali. The halide (5 g.) was added during 20 min.

[1] Wasserman, Aubrey, and Zimmerman, *J. Amer. Chem. Soc.*, 1953, **75**, 96, and refs. therein.
[2] Stevens, Church, and Traynelis, *J. Org. Chem.*, 1954, **19**, 522.
[3] Evans, *Amer. Chem. J.*, 1903, **35**, 115.

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to a stirred, refluxing solution of sodium hydroxide (2 g.) in water (60 ml.) and methanol (25 ml.). The halide quickly disappeared and the solution became deep orange-red. The methanol was boiled off quickly, and the aqueous system was treated as above, to give a very small quantity of solid from which no pure compound was isolated.

Phenacyl alcohol and aqueous alkali. The alcohol [3] (5 g., m. p. 87·5°) was added during 1 hr. to a stirred solution of sodium hydroxide (5 g.) in water (100 ml.) kept at 65—70° in a vessel open to the atmosphere. The solution became orange in the first few min. and a solid separated. Stirring and heating were continued for an additional 1 hr., and the solution was extracted several times with ether (these extracts being discarded), and then acidified. The green oil which separated was discarded and the aqueous solution was extracted several times with ether. Evaporation of these extracts gave crude mandelic acid (2·1 g.), which on recrystallisation gave material (1·5 g.) of m. p. and mixed m. p. 119—120° (depressed on admixture with benzoic acid).

In a separate experiment the alcohol (5 g.) was shaken for 1 min. at room temperature with water (100 ml.) containing sodium hydroxide (10 g.), and the mixture was quickly cooled in ice. The liquid was decanted from the red solid (1·9 g.) which had been formed and was extracted several times with ether and then acidified. The yellow oil (1·9 g.) which separated was taken up in a little ether and the remaining liquid was extracted several times with large volumes of ether to give (±)-mandelic acid (0·3 g.), m. p. 116—118°, mixed m. p. 118—120°, on evaporation.

UNIVERSITY COLLEGE, LEICESTER. [*Received, July 31st,* 1956.]